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CHENNAI

COMPARISON OF COMBINED SPINAL EPIDURAL ANALGESIA WITH EPIDURAL ANALGESIA USING FENTANYL- BUPIVACAINE COMBINATION FOR EFFECTIVE LABOUR ANALGESIA

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MADURAI.

BONAFIDE CERTIFICATE

This is to certify that this dissertation entitled **"COMPARISON OF COMBINED SPINAL EPIDURAL ANALGESIA WITH EPIDURAL ANALGESIA USING FENTANYL BUPIVACAINE COMBINATION FOR EFFECTIVE LABOUR ANALGESIA"** is bonafide work done by **Dr. J. UMA** under our guidance and supervision in the Department of Anaesthesiology, Government Rajaji Hospital, Madurai Medical College, Madurai submitted for the M.D., (Anaesthesiology) BRANCH X EXAMINATION, to be held in March 2008, by the Tamilnadu Dr.M.G.R. Medical University, Chennai.

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DECLARATION

I **Dr. J.UMA** solemnly declare that the dissertation titled "**COMPARISON OF COMBINED SPINAL EPIDURAL ANALGESIA WITH EPIDURAL ANALGESIA USING FENTANYL BUPIVACAINE COMBINATION FOR EFFECTIVE LABOUR ANALGESIA**" has been prepared by me. I also declare that this bonafide work or a part of the work was not submitted by me or any other, for my award, degree, diploma to any other university and board within India or abroad.

This is submitted to The Tamilnadu Dr. M.G.R. Medical University, Chennai in partial fulfillment of the rules and regulations for the award of M.D. (Anaesthesiology) Branch - X to be held in March – 2008.

Place : Madurai

Date : 10-12-2007 **Dr. J. UMA.**

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CONTENTS

INTRODUCTION

"All pain is per se and especially in excess, destructive and ultimately fatal in its nature and effects."

James Young Simpson (1811 – 1870)

"Labour results in severe pain for many women. There is no other circumstance where it is considered acceptable for a person to experience untreated severe pain, amenable to safe intervention, while under a physician's care. Maternal request is a sufficient medical indication for pain relief during labour." Labour results in severe pain for most women. When pain relief is available, the vast majority of women request and receive analgesic medication for the treatment of labour pain. The ideal labour analgesic technique should dramatically reduce the pain of labour, while allowing the parturient to actively participate in the birthing experience. In addition, it should have minimal effect on the foetus or the progress of labour. New labour analgesia techniques approach this goal.

Of all the possible methods of pain relief which can be used in labour, neuraxial blockade (epidural, spinal, CSE, continuous spinal) provides the most effective and least depressant analgesia. Epidural analgesia via a catheter technique provides excellent pain relief and the ability to extend the duration of the block to match the duration of labour, but it is not "instant" in onset and may be associated with motor block. One-shot spinal analgesia using a lipid soluble opioid is rapid and simple, but is associated with a limited duration of action. The combination of epidural and spinal anaesthesia into one technique, termed "CSE" provides the advantages of a spinal (speed of onset, lack of motor block) with the additional flexibility of renewal with an epidural catheter.

Combination of low dose of local anaesthetics and opioid dramatically reduce the incidence of lower limb motor blockade, enabling mothers to walk, sit or stand upright. This was impossible with traditional epidurals using high intermittent boluses of 0.25% bupivacaine which cause a high incidence of motor block in the legs.

AIM

To compare combined spinal epidural analgesia with conventional epidural analgesia using fentanyl-bupivacaine in alleviating labour pain.

To study their effects on the mother and the fetus.

To study their effects on progress of labour and delivery.

HISTORY OF OBSTETRIC ANALGESIA

1. In 1847, shortly after the first public demonstration of ether anaesthesia, ***James Young Simpson*** used diethyl ether for labour analgesia.
2. Repeated injections of large doses of morphine and scopolamine - the technique, called "Da¨mmerschlaf" or "twilight sleep," often led to severe maternal and neonatal respiratory depression.
3. In 1847, ***Walter Channing*** stated that placental transfer of ether was negligible, as he could not detect an odour of ether after having cut the umbilical cord. Although the significance of placental drug transfer was recognized in 1877 when Paul Zweifel proved the presence of chloroform in umbilical vessels of newborns, this knowledge did not alter clinical practice over the next decades.
4. One hundred years ago, in July 1900, the obstetrician ***Oscar Kreis***, from Switzerland was the first to recognize the advantages of regional analgesia in obstetrics, when applying spinal cocaine to ameliorate labour pain in six parturients with a fully dilated cervix.

5. 1923, the first reports on combined spinal-epidural anaesthetics (CSE) in surgical patients appeared, initially as a combined single-shot technique.
6. The basis of regional blocks for labour analgesia was founded on neuroanatomical principles, when ***Cleland*** described the sensory innervation of the uterus in 1933.
7. 1949 Bonica implemented round the clock obstetric services in US.
8. The negative experiences with regional anaesthesia resulted in an abandonment of pain relief in obstetrics until the 1950s, a period often described as the *"dark ages of obstetric anaesthesia"*. It was during this time that "natural childbirth" and "psychoprophylaxis" were widely advocated to avoid serious anaesthesia-related side effects.
9. In the following years, lumbar epidural analgesia gained more popularity because the success rate was high, local anaesthetic requirements were reduced, the onset of analgesia was faster, and the catheter was positioned in a place considered less prone for infection.

10. In 1962, ***Lee*** introduced the first catheter with a closed tip and a lateral hole to reduce trauma on insertion.
11. In 1953 the anaesthesiologist ***V. A. Apgar*** introduced a score to evaluate the newborn based on physiologic variables, thus creating a simple, although not always reliable, tool to detect the effects of anaesthetics on the newborn.
12. The discovery of spinal opioid receptors in the late 1970s led to a widespread use of epidurally and intrathecally administered opioids, and the combination of opioids and dilute local anaesthetics in providing labour pain relief became standard practice. Using these dilute solutions, Chestnut et al. and subsequently Vertommen et al. demonstrated that epidural analgesia did not necessarily increase the incidence of instrumental deliveries.
13. Patient-controlled epidural analgesic techniques, which were shown to reduce local anaesthetic requirements by 30% in comparison with continuous epidural infusions.
14. A potential advantage of CSE is the possibility to ambulate (walking epidural) and has been demonstrated in several trials.

Parturients appreciate not being confined to their beds during the first stage of labour.

15. The first epidural analgesia was done by Leonard. J.Corning in 1885 inadvertently. Lumbar dural puncture was introduced in 1891 by Wytner in England and Quincke in Germany. Karl Gustav August Bier was the first to do a planned spinal anaesthetic in 1898.
16. 1937, Soresi introduced the single space – single needle technique of CSEA.
17. 1979, Curelaru, Swedish anaesthesiologist, introduced the double space – double needle technique of CSEA.
18. 1982 – Coates from England and Mumtaz, Daz & Kuz from Sweden, described the needle through needle technique of CSEA independently.
19. 1990 - Introduction of Eldor needle.
20. Eldor, Coombs & Torrieri technique – Introduction in 1988.

PAIN PATHWAYS IN LABOUR AND DELIVERY:

Pain pathways during labour and delivery

Uterus and cervix - afferent impulses are transmitted via the Aδ and C fibres which travel with sympathetic nerves via the hypogastric plexus to enter the lumbar and lower thoracic parts of the sympathetic chain. Central connection to the spinal cord is via the dorsal root ganglion and lateral division of the posterior roots of T10-L1. Labour pains are therefore referred to the areas of skin supplied by these nerves i.e. the lower abdomen, loins and lumbo-sacral region.

Vagina and pelvic outlet - afferent transmission is also via Aδ and C fibres but with the parasympathetic bundle in the pudendal nerves (S2,3,4). There is also a minor contribution from the ilio-inguinal, genito-femoral and the perforating branch of the posterior cutaneous nerve of thigh.

It is important to appreciate that pain sensitive structures in the pelvis are also involved, i.e. the adnexi, the pelvic parietal peritoneum, bladder, urethra, rectum and the roots of the lumbar plexus. Therefore L2

to S5 must be blocked. There is an overlap and pain relief is not a simple matter of blocking T10 to L1 for the first stage and S2, 3, 4 for the second stage of labour.

CONSEQUENCES OF UNRELIEVED PAIN IN LABOUR

The unrelieved pain in labour produces increased plasma cortisol and catecholamine concentrations which may be responsible for the reduction in utero placental blood flow. Pain induced hyperventilation and hypocapnia can be severe enough in painful labour to produce tetany and it also reduces the uteroplacental blood flow. The respiratory alkalosis further impairs foeto-maternal gas exchange by shifting the oxygen dissociation curve to the left. Foetal PaO2 may fall. When the above stress is removed by effective pain relief all return to normal.

EFFECTS OF LABOUR ANALGESIA USING ABOVE TECHNIQUES ON THE MOTHER:

RESPIRATION:

Uncomplicated CSEA/epidural analgesia has no direct effect on the respiratory center and the changes in pulmonary function caused by it are clinically insignificant. When sensory blockade is at T9 or T10 segment,

there is no weakness of intercostals or abdominal muscles. Even if lower intercostals and abdominal muscles are weakned or paralysed , there is no decrease in pulmonary ventilation because the diaphragm and the unaffected intercostals muscles are able to compensate. If complete motor block extends above T7, there is significant reduction of the expiratory reserve volume and end tidal ventilation falls below the pulmonary closing volume resulting in pulmonary atelectasis and hypoxaemia.

The beneficial effects on ventilation:

During the normal uterine contractions as the frequency and intensity of uterine contractions progresses, moderate to severe pain acts as an intense stimulus to ventilation with consequent reduction in PaCO2 (Respiratory alkalosis).This is followed by hypoventilation and reduction of maternal PaO2 and decreased Foetal PaO2 (Foetal hypoxia). CSEA/Epidural analgesia by eliminating pain prevents or counters the above changes and produces beneficial effects to both mother and fetus.

***CIRCULATION*:**

During painful uterine contraction there is an increase in cardiac output and blood pressure. Above techniques by blunting the painful stimuli and neuroendocrine stress response to pain, reduce the degree of progressive increase in cardiac output and blood pressure. This decreases the myocardial workload and oxygen consumption. With the uppermost level of analgesia at T10, there is decrease in peripheral resistance, venous return and cardiac output.In normal parturient lying on their side, reflex cardiovascular mechanism counteract these effects and maintain blood pressure near normal levels.

***NEUROENDOCRINE RESPONSE*:**

Pain increases neuroendocrine stress hormones. CSEA/Epidural analgesia by blocking all nociceptive input and sympathetic effects, reduce the release of stress hormones thereby preventing untoward effects on the cardiovascular system and the progress of labour. It doesn't decrease the Foetal catecholamines and beta-endorphin release.

ALIMENTARY FUNCTION:

CSEA/Epidural analgesia by interrupting the nociceptive barrage and sympathetic efferents to gastrointestinal tract decreases the magnitude of gastrointestinal inhibition and tends to increase the lower oesophageal sphincter tone. Intrathecal /Epidural opioids tends to delay gastric emptying.

ON THE FOETUS AND NEWBORN:

CSEA/ epidural analgesia stabilizes the maternal physiology though such mechanisms that include decreased maternal oxygen consumption, higher maternal PaO2, less maternal acidosis, and less catecholamine release, all providing for a favourable intrauterine environment. Neonates of mothers managed with properly placed CSEA/epidural analgesia did not manifest the neonatal depression. Widespread use of segmental epidural analgesia entails the use of smaller dose of local anaesthetic and there is minimal or no adverse effects on the parameters that constitute the APGAR score. Non-ionised portion of local anaesthetic crosses the placental membranes but the percentage of bupivacaine that crosses the placenta -18% is less when compared with other local anaesthetics.

Foetal tissue uptake of local anaesthetics will increase with increasing degrees of foetal acidosis .Foetal and maternal blood gases and acid base status during either low dose intermittent or continuous lumbar epidural analgesia was not significantly different from those without analgesia. Increase in uteroplacental blood flow and improvement in foetal acid base status following CSEA/epidural analgesia is due to relief of vasospasm of the uteroplacental circulation and elimination of sympathoadrenal activity. It has no effect on foetal heart rate patterns and on neurobehavioural responses of neonate.

ON UTERINE CONTRACTILITY:

1) If maternal hypotension and hypovolemia are avoided and the mother assumes left lateral position, above techniques will not lead to a change in frequency or strength of uterine contractions
2) Increased uteroplacental blood flow with CSEA/epidural analgesia itself may increase uterine action
3) CSEA/ epidural analgesia normalizes the irregular contraction in inco-ordinate uterine action and speeds up labour.

ON THE STAGES OF LABOUR

FIRST STAGE: The refined technique of CSEA/ EA has little or no effect on the progress of cervical dilatation and the duration of the first stage of uncomplicated labour. Care should be taken that the analgesia is initiated at the appropriate time with adequate preloading. The mother is kept in the left lateral position during intermittent bolus administration of drug and throughout labour so that maternal hypotension is avoided and uteroplacental blood flow is maintained. The first stage is divided into latent and active phases. The active phase has three identifiable component parts- an acceleration phase, a linear phase of maximum slope and a deceleration phase. The maximum cervical dilatation occurs during the active phase and the intensity of pain is also severe in this stage.

LATENT PHASE: Initiation of CSEA/ EA or even excessive sedation during this phase decreases uterine activity and prolongs the labour.

ACTIVE PHASE: CSEA/Epidural analgesia does not alter the overall rate of progress in the active phase of the first stage of normal labour. It may actually shorten the first stage of labour by abolishing anxiety.

SECOND STAGE: The effect of CSEA/ EA on the resistant and expulsive forces and hence on the duration of the second stage of labour depends on the technique used and obstetric management.

Continuous caudal or mid lumbar is associated with significantly prolonged second stage of labour and increased incidence of instrumental delivery.

The use of segmental epidural analgesia for the first stage and **its** extension to the sacral segments for the second stage and delivery with 0.125 bupivacaine or 1% lignocaine still shows longer duration of second stage and increased incidence of instrumental delivery. The second stage is prolonged because-

1) Block of the sensory roots S 2,3,4 obtunds the bearing down reflex.
2) The partial block of the lower abdominal muscles weaken them thereby decreasing the maternal expulsive power.
3) The associated weakening of the pelvic floor muscles delay the rotation of the presenting part during its descent through the pelvis and this also contributes to the delay in the second stage.

4) CSCA Epidural analgesia interferes with Ferguson's reflex and the release of oxytocin from the posterior pituitary in response to stretching of birth canal. This can be overcome by a routine use of oxytocin infusion especially in primipara.
5) Delay in bearing down efforts until the presenting part is visible at the introitus is likely to prolong the second stage. But if foetal monitoring shows no distress and maternal distress is not allowed, it will decrease significantly the incidence of non-rotation and increase of the incidence of spontaneous delivery.
6) CSEA/epidural analgesia has beneficial effects in dysfunctional uterine contractions. It improves maternal and Foetal outcome.

THIRD STAGE: Third stage is not affected by CSEA/EA.

DELIVERY PROCESS: The optimal management of prolonged second stage of labour remains a confused area of thought and action. As the second stage is prolonged there is a tendency for the obstetricians to apply forceps early. But given sufficient time and in the absence of anatomical obstruction, the foetal head will rotate satisfactorily. If the mother is not allowed to bear down until the presenting part distends the perineum she

will have sufficient reserve of power and will to push effectively to accomplish a spontaneous delivery. If as delivery approaches, uterine activity appears not to be sufficient to maintain the steady onward progress of the presenting part, it can be supplemented by judicious administration of oxytocin. Crawford stresses that if there is no evidence of foetal distress and if the mother displays no sign of undue fatigue, there is no recognizable limit to the time which can be invested in the delivery process.

SPINAL EPIDURAL SPACE – IN PREGNANCY

Epidural veins

The epidural venous plexus is a valveless system that communicates with the basivertebral vein, the intracranial sigmoid, occipital, and basilar venous sinuses and the azygos system. Drugs, air or other material injected into the epidural space can potentially reach the heart or brain directly through this route. Abdominal and thoracic veins connect with the venous plexus through the intervertebral foramina and transmit intraabdominal and intrathoracic pressure to the epidural space. Inferiorly, the venous plexus connects with the iliac veins through the

sacral venous plexus. Obstruction of the inferior vena cava in late trimester pregnancy can distend the epidural venous plexus, with important implications for spinal and epidural anaesthesia. This increases the risk of intravascular cannulation with an epidural catheter.

It effectively decreases epidural space volume, allowing local anaesthetics to distribute more widely with resulting greater degrees of block. Exposure to greater vascular surface area also potentially increases the risk for local anaesthetic toxicity due to absorption from the epidural space. The constituents of cerebral spinal fluid (CSF) do not change during pregnancy but its volume is reduced due to compression from the epidural veins in the epidural space. The pressure of the CSF is therefore increased. Between contractions the pressure may be around 28 mm Hg but during painful contractions it may rise to as much as 70mmHg. It is therefore probably safer not to advance an epidural or spinal needle during contractions for risk of puncturing the dura and expulsion of CSF at high pressure. As a result of reduced volume of CSF drug dose requirement is reduced to one third on normal for neuraxial blocks in late pregnancy.

CONDITIONS ESSENTIAL FOR INITIATING SPINAL-EPIDURAL ANALGESIA:

1. The parturient should be in the active phase of labour and experiencing moderate pain during uterine contractions
2. The contractions should be regular, of good intensity and occurring at intervals of 3 minutes or less and lasting 35-40 seconds or longer.
3. The presenting part should be engaged in the pelvis.
4. The cervix should be dilated 3 or 4 cm.

INDICATIONS FOR SPINAL-EPIDURAL ANALGESIA:

1. To relieve labour pains thereby reducing anxiety and apprehension in expectant mothers.
2. Maternal factors – Trial of labour in high risk parturients

Congenital or acquired heart disease/Pregnancy induced hypertension / Essential hypertension and pulmonary hypertension/Endocrine disorders like diabetes/Renal and hepatic diseases/Pulmonary diseases like asthma and neurological disorders.

3. **Foetal conditions**

Prematurity/Postmaturity/Multiple births/Breech deliveries and intra-uterine growth retardation.

4. **Obstetric conditions**

Prolonged labour due to primary cervical dystocia/Induction of labour/Forceps delivery/Multiple pregnancies and occipito-posterior position.

CONTRA-INDICATIONS FOR LUMBAR SPINAL-EPIDURAL ANALGESIA:

Absolute:

Patient refusal / Infection at site of proposed puncture / coagulopathies /anatomical abnormalities like spina bifida, fused spine or AV malformations diagnosed at the lumbar vertebral column and severe hypovolemia from hemorrhage, dehydration or malnutrition.

Relative:

Very early labour/Rapid or precipitous labour/Unco-operative patient/Uncontrolled pre-eclampsia, eclampsia, accidental hemorrhage and pre-existing neurological diseases.

COMPLICATIONS ANTICIPATED:

Systemic arterial hypotension, Systemic toxic effects due to local anaesthetics, Perforation of dura- postdural puncture headache, Total spinal anaesthesia due to accidental sub-arachanoid injection of large doses of local anaesthetics, Shearing of catheters, Local or epidural infection or possible abscess or extradural hematoma, Shivering, Neurological sequelae-backache, leg pain, numbness and weakness, Foetal or neonatal complications (Maternal hypotension, Excess amounts of local anaesthetic, Accidental Foetal local anaesthetic intoxication, Injection of local anaesthetic into Foetal scalp with caudal analgesia) and Complications due to intrathecal/epidural opioids (Pruritis, Nausea and vomiting, Urinary retention, Delayed respiratory depression and Sedation)

PHARMACOLOGY:

BUPIVACAINE:

It was first synthesized in Sweden by Ekenstam and his colleagues in 1957 and used clinically by L.J.Telivuo in 1963.

Chemical formula	C18H28N20
Molecular mass	288.43 g/mol

PHARMACOKINETIC DATA

pKa	8.1		
Lipid solubility	28	Protein binding	95%
Nonionised fraction at physiological pH			15%

Onset of action	1-2 minutes (intrathecal)
	15-20 minutes (epidural)
Volume of distribution	73 litres
Clearance of drug from plasma	0.47 litres/minute
Distribution half life – alpha	2.7 minutes
- beta	28 minutes
Elimination half life (neonates)	3.5 hours (adults), 8.1 hours
Metabolism	Hepatic
Excretion	Renal, 4 to 10%
Toxic concentration	>1.6 mcg/ml

THERAPEUTIC CONSIDERATIONS

Pregnancy	Category A
Routes	- Spinal, epidural, caudal, regional nerve blocks, topical
Maximum dose	- 3mg/kg with or without adrenaline

Bupivacaine is chemically designated as 2-piperidinecarboxamide, 1-butyl-N-(2, 6-dimethylphenyl)-, monohydrochloride, monohydrate.

Bupivacaine is related chemically and pharmacologically to the aminoacyl local anaesthetics. It is an amide type of local anaesthetic agent. It is a homologue of mepivacaine and is chemically related to lidocaine. All three of these anaesthetics contain an amide linkage between the aromatic nucleus and the amino or piperidine group. They differ in this respect from the procaine-type local anaesthetics, which have an ester linkage. Solutions should be stored at controlled room temperature 15-30°C (59-86°F) . Solutions containing epinephrine should be protected from light.

Preservative free: MPF indicates single dose solutions that are Methyl Paraben Free . It is a sterile isotonic solution containing sodium chloride.

Mechanism of action

Bupivacaine binds to the intracellular portion of sodium channels and blocks sodium influx into nerve cells, which prevents depolarization. In general, the progression of anaesthesia is related to the diameter, myelination and conduction velocity of affected nerve fibers. Clinically,

the order of loss of nerve function is as follows: (1) pain, (2) temperature, (3) touch, (4) proprioception, and (5) skeletal muscle tone. Since pain transmitting nerve fibres tend to be thinner and either unmyelinated or lightly myelinated, the agent can diffuse more readily into them than into thicker and more heavily myelinated nerve fibres like touch, proprioception, etc. (Myelin is non-polar / lipophilic).

Developments

Levobupivacaine is the *R* (-)-enantiomer of bupivacaine, with a longer duration of action and produces less vasodilatation

PHARMACOKINETICS:

The rate of systemic absorption of local anaesthetics is dependent upon the total dose and concentration of drug administered, the route of administration, the vascularity of the administration site and the presence or absence of epinephrine in the anaesthetic solution. A dilute concentration of epinephrine (1:200,000 or 5 mcg/mL) usually reduces the rate of absorption and peak plasma concentration, permitting the use of moderately larger total doses and sometimes prolonging the duration of action. The onset of action is rapid in pregnancy and anaesthesia is long

lasting. The duration of anaesthesia is significantly longer. It has also been noted that there is a period of analgesia that persists after the return of sensation, during which time the need for strong analgesics is reduced.

Local anaesthetics appear to cross the placenta by passive diffusion. The rate and degree of diffusion is governed by - the degree of plasma protein binding, the degree of ionization and the degree of lipid solubility.

Foetal/maternal ratios of local anaesthetics appear to be inversely related to the degree of plasma protein binding, because only the free, unbound drug is available for placental transfer. Bupivacaine with a high protein binding capacity (95%) has a low Foetal/maternal ratio (0.2 to 0.4). Depending upon the route of administration, local anaesthetics are distributed to some extent to all body tissues, with high concentrations found in highly perfused organs such as the liver, lungs, heart and brain.

After injection for caudal, epidural, or peripheral nerve block in man, peak levels of bupivacaine in the blood are reached in 30 to 45 minutes, followed by a decline to insignificant levels during the next three to six hours. Various pharmacokinetic parameters of the local anaesthetics can be significantly altered by the presence of hepatic or renal disease,

addition of epinephrine, factors affecting urinary pH, renal blood flow, the route of drug administration, and the age of the patient. The half-life of bupivacaine in adults is 2.7 hours and in neonates 8.1 hours.

Amide-type local anaesthetics such as bupivacaine are metabolized primarily in the liver via N-dealkylation and conjugation with glucuronic acid. The major metabolite of bupivacaine is 2, 6-pipecoloxylidine. Patients with hepatic disease, especially those with severe hepatic disease, may be more susceptible to the potential toxicities of the amide-type local anaesthetics.

The kidney is the main excretory organ for bupivacaine and its metabolites. Urinary excretion is affected by renal perfusion and factors affecting urinary pH. Only 5% of bupivacaine is excreted unchanged in the urine.

Indications: Bupivacaine is indicated for local anaesthesia including infiltration, nerve block, epidural, and intrathecal anaesthesia and analgesia.

Contraindications: Bupivacaine is contraindicated for IV regional anaesthesia (IVRA) because of potential risk of tourniquet failure and systemic absorption of the drug and known allergy to bupivacaine.

Adverse CNS effects:

CNS effects usually occur at lower blood plasma concentrations and additional cardiovascular effects present at higher concentrations, though cardiovascular collapse may also occur with low concentrations.

CNS excitation can manifest as nervousness, tingling around the mouth, tinnitus, tremor, dizziness, blurred vision, seizures followed by manifestation of CNS depression - drowsiness, loss of consciousness, respiratory depression and apnoea.

Other central nervous system effects are nausea, vomiting, chills, and constriction of the pupils.

The incidence of convulsions associated with the use of local anaesthetics varies with the procedure used and the total dose administered. In a survey of studies of epidural anaesthesia, overt toxicity progressing to convulsions occurred in approximately 0.1% of local anaesthetic administrations

Neurologic

Neurologic effects following epidural or caudal anaesthesia may include - spinal block of varying magnitude (including high or total spinal block); hypotension secondary to spinal block; urinary retention; fecal and urinary incontinence; loss of perineal sensation and sexual function; persistent anaesthesia, paresthesia, weakness, paralysis of the lower extremities and loss of sphincter control, all of which may have slow, incomplete or no recovery; headache; backache; septic meningitis; meningismus; slowing of labour; increased incidence of forceps delivery; or cranial nerve palsies due to traction on nerves from loss of cerebrospinal fluid.

Cardiovascular effects :

Hypotension, bradycardia, decreased cardiac output, dose dependant depression of myocardium, arrhythmias, cardiac arrest

Allergic:

Allergic type reactions are rare and may occur as a result of sensitivity to the local anaesthetic, to other formulation ingredients, such as the antimicrobial preservative methylparaben contained in multiple dose vials or sulfites in epinephrine-containing solutions.

These reactions are characterized by signs such as urticaria, pruritus, erythema, angioneurotic edema (including laryngeal edema), tachycardia, sneezing, nausea, vomiting, dizziness, syncope, excessive sweating, elevated temperature, and possibly, anaphylactoid symptomatology (including severe hypotension).

- Cross sensitivity among members of the amide-type local anaesthetic group has been reported.
- The usefulness of screening for sensitivity has not been definitely established.

Labour and Delivery.

Local anaesthetics rapidly cross the placenta, and when used for epidural, caudal or pudendal block anaesthesia, can cause varying degrees of maternal, foetal and neonatal toxicity. Local anaesthetics produce vasodilation by blocking sympathetic nerves and may produce maternal hypotension. Epidural, caudal, or pudendal anaesthesia may alter the forces of parturition through changes in uterine contractility or maternal expulsive efforts. Epidural anaesthesia has been reported to prolong the second stage of labour by removing the parturient's reflex urge to bear

down or by interfering with motor function. The use of obstetrical anaesthesia may increase the need for forceps assistance.

Nursing Mothers: Bupivacaine has been reported to be excreted in human milk suggesting that the nursing infant could be theoretically exposed to a dose of the drug.

FENTANYL:

Fentanyl is an opioid analgesic, first synthesized by Janssen Pharmaceutica (Belgium) in the late 1950s, with a potency 75 to 100 times that of morphine. Fentanyl was introduced into medical practice in the 1960s. The chemical name of fentanyl is *N*-phenyl-*N*-(1-phenethyl-4-piperidinyl) propanamide.

Molecular mass	336.471 g/mol
Melting point	87.5 degrees Celsius

THERAPEUTIC CONSIDERATIONS

Pregnancy	Category C
Routes	Intravenous, intramuscular, transdermal, buccal, sublingual, oral, intrathecal, epidural.

The LD_{50} in humans, by intravenous injection, is 0.2-1 milligrams.

Analogues

- Alfentanil, an ultra-short acting (5–10 minutes) analgesic,
- Sufentanil , a potent analgesic (5 to 10 times more potent than fentanyl) .
- Remifentanil , currently the shortest acting opioid, has the benefit of rapid offset, even after prolonged infusions.
- Carfentanil , an analogue of fentanyl with an analgesic potency 10,000 times that of morphine and is used in veterinary practice to immobilize certain large animals.

Mechanism of Action

Binds with stereo specific receptors – mu 2 receptor agonist at many sites within the CNS and other tissues. It prevents the release of endogenous opioids- beta endorphin and increases pain threshold, alters pain reception, inhibits ascending pain pathways.

PHARMACOKINETIC DATA

Protein binding	80-85%
Lipid solubility	High

Distribution	Highly lipophilic, redistributes into muscle and fat
Metabolism	Hepatic, CYP3A4
Onset	5 to 9 minutes
Duration	I.M: 1-2 hours, I.V: 0.5-1 hour, Transmucosal: Related to blood level.
Half life	3 to 12 hours (average 7 hours)
Excretion	Urine (primarily as metabolites, less than 8% as unchanged drug)

Metabolism: Hepatic, primarily via CYP3A4. Extensively metabolized by N-dealkylation, hydroxylation and amide hydrolysis to inactive metabolites including norfentanyl and despropionyl norfentanyl and excreted via bile and urine. Fentanyl is significantly more lipid-soluble, compared to morphine and, relative to morphine, has a more rapid onset of action .It is also a weak base and at physiological pH only about 10% of molecules are un-ionized. Clearance of about 10-20 ml/kg/minute is consistent with a primary hepatic mechanism. Fentanyl's short duration of action following bolus administration is explained by rapid redistribution from brain to other compartments such as skeletal muscle and fat. If, however, fentanyl is administered by continuous IV

infusion or multiple IV dosing, other non- CNS compartments will get saturated and the remaining CNS fentanyl will contribute to postoperative ventilatory depression.

Therapeutic use

Fentanyl is extensively used for anaesthesia and analgesia, most often in the operating room and intensive care unit for the purpose of, premedication—1-2mcg/kg IM 30-60 minutes prior to induction, analgesia—1-4mcg/kg IV, to blunt circulatory responses – 5-10mcg/kg IV, large doses of fentanyl—50-100mcg/kg IV to produce surgical anaesthesia, narcotic supplementation for general anaesthesia and regional anaesthesia, obstetric analgesia and neuroleptanalgesia with droperidol.

Fentanyl transdermal patch –50-100mcg/hour used in chronic pain management. Fentanyl patches work by releasing fentanyl into body fats, which then slowly release the drug into the blood stream over 72 hours, allowing for long lasting relief from pain

Fentanyl lozenges are solid formulation of fentanyl citrate on a stick in the form of a lollipop that dissolves slowly in the mouth for

transmucosal absorption. These lozenges are intended for opioid-tolerant individuals and are effective in treating breakthrough pain.

The development of small fentanyl buccal pellets may be much more practical. These are effervescent tablets placed in the cheek and are absorbed through the buccal mucosa. One advantage of such tablets is claimed to be quicker absorption into the bloodstream at lower dosage levels.

Fentanyl is frequently given intrathecally as part of spinal anaesthesia and analgesia or epidurally for epidural anaesthesia and analgesia. It is also used as a sedative.

Adverse effects

Like other lipid soluble drugs, the pharmacodynamics of fentanyl are poorly understood. Fentanyl has a therapeutic index of 270.

Cardiovascular: Hypotension, bradycardia, cardiac arrhythmia, oedema, orthostatic hypotension, hypertension, syncope.

Respiratory: Respiratory depression, apnea, bronchitis, dyspnea, hemoptysis, pharyngitis, rhinitis, sinusitis, upper respiratory infection.

The precise reason for sudden respiratory depression is unclear, but there are several hypotheses:

- Saturation of the body fat compartment in patients with rapid and profound body fat loss (patients with cancer, cardiac or infection-induced cachexia can lose 80% of their body fat).
- Early carbon dioxide retention causing cutaneous vasodilatation (releasing more fentanyl), together with acidosis which reduces protein binding of fentanyl (releasing yet more fentanyl).
- Reduced sedation, losing a useful early warning sign of opioid toxicity, and resulting in levels closer to respiratory depressant levels.

Central nervous system: CNS depression, confusion, drowsiness, sedation, abnormal dreams, abnormal thinking, agitation, amnesia, dizziness, euphoria, fatigue, fever, hallucinations, headache, insomnia, nervousness, paranoid reaction.

Gastrointestinal: Nausea, vomiting, constipation, xerostomia, abdominal pain, anorexia, biliary tract spasm, diarrhoea, dyspepsia, flatulence.

Neuromuscular & skeletal: Chest wall rigidity (high dose I.V.), weakness, abnormal coordination, abnormal gait, back pain, paresthesia, rigors, tremor.

Miscellaneous: Miosis Diaphoresis, Hiccups, flu-like syndrome, speech disorder.

Dermatologic: Erythema, papules, pruritus, rash, urticaria

Local: Application site reaction

Over dosage/Toxicology

Symptoms of overdose include CNS depression, respiratory depression, and miosis. Treatment is supportive. Naloxone, 2 mg I.V. with repeat administration as necessary up to a total of 10 mg, can also be used to reverse toxic effects of the opiate. Patients who experience adverse reactions during use of transdermal fentanyl should be monitored for at least 24 hours after removal of the patch.

Drug Interactions

Substrate of CYP3A4 (major); **Inhibits** CYP3A4 (weak)

CNS depressants: Increased sedation with CNS depressants, phenothiazines

CYP3A4 inhibitors: May increase the levels/effects of fentanyl. Potentially fatal respiratory depression may occur when a potent inhibitor is used in a patient receiving chronic fentanyl (eg. transdermal). Example of inhibitors include azole antifungals, ciprofloxacin, clarithromycin, diclofenac, doxycycline, erythromycin, imatinib, isoniazid, nefazodone, nicardipine, propofol, protease inhibitors, quinidine, and verapamil.

MAO inhibitors: Not recommended to use fentanyl within 14 days. Severe and unpredictable potentiation by MAO inhibitors has been reported with opioid analgesics.

Pregnancy Implications: Category C/D. Fentanyl crosses the placenta and has been used safely during labour. Chronic use during pregnancy has shown detectable serum levels in the newborn with mild opioid withdrawal.

Lactation : Enters breast milk/not recommended (American Academy of Paediatrics rates "compatible").

Contraindications: Hypersensitivity to fentanyl or any component of the formulation. severe respiratory disease or depression.

EFFECT OF COMBINATION OF LOW CONCENTRATIONS OF BUPIVACAINE WITH OPIOID:

Low concentrations of local anaesthetics placed neuraxially blocking conduction by A delta fibres and also inhibiting sympathetic nerve transmission. Opiates administered neuraxially produce a selective block of nociceptive pathways, blocking pain transmission via the C fibres more readily than A delta fibres. Combination of low concentration of local anaesthetics with low dose opioids eliminate pain via a combined and possible synergistic mechanism by working at two distinct sites- local anaesthetic at the nerve axon and the opioid at the spinal level.

1) Faster in onset
2) Intense and long lasting sustained analgesia
3) Provides excellent analgesia during first stage of labour without affecting uterine contractility
4) Tendency to decrease the duration of active phase of first stage of labour
5) Addition of opioids significantly decreases the amount of opioids required

REVIEW OF LITERATURE

1. CSE analgesia for labour is usually achieved using a short-acting lipid soluble narcotic such as fentanyl or sufentanil. Although pruritus is associated with lipid soluble opioids, it is usually mild and short lived and does not generally need to be treated. Advances in labour analgesia **David J. Birnbach, MD** *Canadian Journal of Anaesthesia* 51:R12 (2004)
2. Of all the possible methods of pain relief which can be used in labour, neuraxial blockade (epidural, spinal, CSE, continuous spinal) provides the most effective and least depressant analgesia. The combination of epidural and spinal anaesthesia into one technique, termed "CSE" provides the advantages of a spinal (speed of onset, lack of motor block) with the additional flexibility of renewal with an epidural catheter .Advances in labour analgesia **David J. Birnbach, MD** *Canadian Journal of Anaesthesia* 51:R12 (2004)
3. CSE provides better pain relief in the early stages after insertion. Comparative Obstetric Mobile Epidural Trial (COMET) Study

Group. Randomized controlled trial comparing traditional with two "mobile" epidural techniques. Anesthesiology 2002; 97: 1567–75.

4. A review of the complications associated with CSE has concluded that CSE is as safe a technique as a conventional epidural technique and is associated with greater patient satisfaction. **Norris MC, Grieco WM, Borkowski M, et al.** Complications of labour analgesia: epidural versus combined spinal-epidural techniques. *Anesth Analg 1995; 79: 529–37.*

5. We conclude that intrathecal bupivacaine 1.25 mg with fentanyl 25 micrograms provided analgesia of similar onset and quality compared with bupivacaine 2.5 mg and fentanyl 25 micrograms. Although the duration of analgesia was shorter, the incidences of motor block and hypotension were less with the smaller dose. *Br J Anaesth. 1999 Dec;83(6):868-71*. Combined spinal-epidural analgesia in labour: comparison of two doses of intrathecal bupivacaine with fentanyl. **Lee BB, Ngan Kee WD, Hung VY, Wong EL**. Department of Anaesthesia and Intensive Care, Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, China.

6. The combined spinal epidural analgesia will only result in significant falls in systolic blood pressure within 30 minutes of the spinal injection. No further important changes in blood pressure occur when mobilising or with epidural top-ups. The combined spinal epidural analgesia may modify the normal compensatory mechanisms of blood pressure control, but does not cause significant maternal hypotension once the spinal injection has been given: *Br J Obstet Gynaecol. 1995 Mar;102(3):192-7.* Blood pressure changes during labour and whilst ambulating with combined spinal epidural analgesia. **Shennan A, Cooke V, Lloyd-Jones F, Morgan B, de Swiet M.** Queen Charlotte's and Chelsea Hospital, London.
7. **R. Fernando et al (1997)** have used low dose combination of bupivacaine – fentanyl combination for labour analgesia, in the form of combined spinal epidural analgesia. He concluded that the combination of drugs resulted in smaller levels of drug in both mother and neonate and is of little clinical significance in contrast to intramuscular pethidine which has longer acting neonatal effects.

8. **David J Birnbach** in the *New England Journal of Medicine (1997)* reported that combined spinal epidural analgesia combining the intrathecal administration of an opioid drug through a fine spinal needle with the subsequent epidural administration of low dose mixtures of local anaesthetic and opioid drugs through a catheter resulted in faster onset analgesia, decreased motor block(thus allowing them to walk) and a greater sense of control.
9. **Curelaru** "The advantage of CSEA is the possibility of obtaining a high quality conduction anaesthesia, unlimited in time …". Long duration sub-arachnoid anaesthesia with continuous epidural block. Prktische Anasthesie Wider belelung and Intensivtherapie 1979;14:71-78.
10. Anaesthesiologists were more inclined to using CSE than EA for multiparous parturients in a more painful advanced stage of labour. Patient satisfaction was higher for CSE. **A T Sia and colleagues**, Neuraxial Block for Labour Analgesia, *Singapore Med J 2003 Vol 44 (9) : 464-470.*
11. Combined spinal – epidural analgesia has the advantages of faster onset of analgesia, decreased motor block and a greater sense of

control. **The New England Journal of Medicine,** *Vol 337:1764-1766*.

12. Epidural analgesia with a low concentration of local anaesthetic and opioid mixture takes longer to produce complete analgesia, it is a satisfactory alternative to CSE. **David L. Hepner, MD and collogues.**

13. Labor progress and outcome are similar among women receiving either combined spinal-epidural or epidural analgesia and not associated with an increased frequency of anaesthetic complications. **Mark C Norris MD and colleagues.** Combined Spinal – Epidural versus Epidural Labor Analgesia *Anaesthesiology 2000;95:913-20.*

14. Opioids administered in combination with local anaesthetics have a synergistic effect with various local anaesthetic agents, reducing the ED. However is associated with an increased incidence of pruritus. **Marc Van De Velde,** *European Society of Anaesthesiologists, Drug Combinations inRegional Analgesia During Labou, Sunday June6,2004.*

15. Any epidural has the potential to be a “walking epidural”. As motor block will imede the woman’s ability to ambulate, more dilure solutions of local anaesthetic are used and combined with an opioid such as fentanyl. Obstetric Guideline Pain Management During Labour, *British Columbia Reproductive Care Program.*
16. the combination of spinal opioids with subsequent epidural analgesia has been suggested to provide the best of both techniques: rapid onset of analgesia with a minimal drug dose, followed by great flexibility of continuous analgesia. *Anesthesiology Vol 91(1); July 1999 : pp299-302.*

MATERIALS AND METHODS

The study was conducted at Government Rajaji Hospital, Madurai attached to Madurai Medical College, Madurai. The study was conducted between September 2005 and June 2007.

A pilot study was conducted on a small group of patients before the actual study in order to assess the feasibility of the study, to understand the needs and demands of out population to be studied, to assess the drug requirements of bupivacaine and fentanyl in our population.

Based on the pilot study, the concentration of bupivacaine and the dose of fentanyl was decided and the main study was proceeded.

The study involved 75 parturients in active labour with term gestation, belonging to ASA I class with singleton pregnancies with vertex presentation and no cephalo-pelvic disproportion.

Exclusion Criteria : Parturient with cardiac or respiratory diseases, spinal deformities, local skin sepsis, coagulopathies, parturients who have received systemic opioids early in labour, parturient refusal, pre-eclampsia, anaemia complicating pregnancy, multiple gestation, breech presentation, previous caesarean section and known H/O allergy to local anaesthetics and / or fentanyl.

A written informed consent was obtained from both the study group after explaining the procedure in detail.

75 cases were selected at random and grouped into 25 in the combined spinal epidural analgesia group (CSEA), 25 in the epidural analgesia group (EA) and 25 in the control group Each group in turn included 12 primigravida and 13 multigravidae. The above sub-grouping was done as the primi and multigravidae behave entirely different in the labour process and progress. All the study groups were well matched in terms of age, height, weight, parity and labour characteristics.

The following resuscitative equipment were kept ready before the start of the procedure to treat complications if any that could occur - anaesthesia machine with full oxygen supply, airways of different sizes, laryngoscope with appropriate size blades, endotracheal tubes of appropriate sizes, laryngeal mask airways of appropriate sizes, McCoy laryngoscope blade and bougie, functioning suctioning apparatus, Inj. Thiopentone or benzodiazipine for the treatment of possible convulsions. Inj. Ephedrine for treatment of hypotension, Inj. Atropine for treatment of bradycardia, Inj. Naloxone for the treatment of opioid induced respiratory

depression and other intractable side effects and emergency drug tray with all essential drugs.

For initiating epidural block, the following were kept ready:- Draping towels and sponge holding forceps, sterile gauze pieces in kidney tray, bowls with antiseptic solution, 18 G Tuohy needle with 20 G portex epidural catheter with filter and loss of resistance syringe for single use, 2 ml syringe with 24 G needle for local anaesthetic infiltration, 5 ml and 10ml syringe with needles to draw up fentanyl and bupivacaine respectively, Inj. Bupivacaine – 0.25% preservative free vial, Inj. Lignocaine – 2% vial, Inj. Fentanyl ampoules, distilled water, saline and metal files to open ampoules, delivery tray, baby resuscitation tray and waterproof adhesive plasters.

For initiating combined spinal epidural block in addition to above 27 G Quincke needle was kept ready.

Technique of Epidural Analgesia

Following parturient selection a through evaluation of her medical and obstetric condition was done. Physical examination included examination of pulse rate, blood pressure, respiratory rate, SpO2,

cardiovascular, central nervous system and respiratory system examination. Back of the parturient was examined to rule out local skin sepsis, spina bifida or kypho-scoliosis. Parturients height and weight were recorded. Description of the 10 point linear visual analogue scale (VAS) was given. Obstetrician recorded the nature of the uterine contraction, cervical dilatation, station of the Foetal head and the foetal heart rate.

An intravenous line was set up and 500ml of lactated Ringers solution was started. Pulse oximeter and non invasive blood pressure monitoring were used in order to note the arterial oxygen saturation, pulse rate and blood pressure.

Parturient was placed in lateral position on a horizontal table. Under strict aseptic precautions L2-3/L3-4 epidural space was identified by loss of resistance to saline technique with 18 G Tuohy epidural needle.

Epidural catheter was inserted through the needle. Test dosing was done using 3ml of 1.5% lignocaine with 1:2,00,000 adrenaline to rule out intravascular and intrathecal placement of catheter and fixed by sterile dressing and water proof adhesive plasters.

The parturients were positioned supine with left uterine displacement. After negative aspiration for blood and cerebrospinal fluid,

10ml of 0.125% preservative free bupivacaine with 2 μcg/ml of Inj. Fentanyl was given initially.

Top ups of above dosage were given at the end of every one hour since previous dosage. The top up volume was reduced to 6-8ml if there was significant hypotension, bradycardia or sedation.

Technique of combined spinal epidural analgesia using double needle, double space / interspace method:

Pre procedure preparation was same as for epidural group.

Under strict aseptic precautions sub-arachanoid space is entered at L3-4/L2-3 interspace using 27 G Quincke spinal needle.

25 μcg of Inj. Fentanyl with 0.5ml of preservative free 0.25% bupivacaine was injected intrathecally

- Subsequent identification of the epidural space one space above spinal injection, catheter placement and fixation were proceeded with, as in epidural group.
- First epidural dose of 10ml of 0.125% preservative free bupivacaine with 2μcg of Inj. Fentanyl was given 45 minutes after intrathecal fentanyl administration.

- Subsequent top ups of same or reduced dosage based on heart rate, blood pressure and sedation are administered at the end of every hour since previous dosing.

Both the Groups

- All epidural top ups were given in 2-3ml increments at 1-2 minute intervals (maximum of 10ml/hr).
- Any breakthrough pain (VAS >4) managed with 6-8ml of same drug mixture.
- Depending upon parturient need the obstetrician was allowed to use artificial rupture of membranes, Inj. Oxytocin for acceleration etc.
- During the second stage of labour, the parturients were encouraged to bear down.
- Episiotomy and episiotomy repair were preceeded by local anaesthetic infiltration since above combination of low concentration bupivacaine and fentanyl does not provide surgical plane of analgesia.

Monitoring

1. Blood pressure every 2 minutes for the first 15 minutes after giving loading dose and then every 10 minutes.
2. Continuous maternal and foetal heart rate and maternal SpO2 monitoring
3. Continues verbal communication with the parturient in order to assess pain relief.
4. The time of onset of analgesia was noted. Parturients were asked to mark a point on the 10 point linear visual analogue scale (VAS) every 15 minutes to evaluate the adequacy of pain relief which was graded by Elbaz 1984.

   If VAS score was >4, it was considered to be breakthrough pain and additional epidural top up dose was given as mentioned earlier.
5. The level of sensory analgesia and intensity of motor blockade were assessed at half hourly intervals.

   Motor block : Bromage scale (BONICA – 1995)

   0 - No block (10%) - Full flexion of knees and feet possible

1 - Partial (33%) - Just able to flex knees, still full flexion of feet possible.

2 - Almost complete (66%) – Unable to flex knees, still full flexion of feet possible

3 - Complete - Unable to move legs or feet

6. The total dose of bupivacaine and fentanyl administered were noted in each group.

7. Complications : Pruritis, sedation, urinary retention, nausea, vomiting, shivering, headache, backache, hypotension, bradycardia and respiratory depression were noted.

Sedation score:

0 - Fully awake and oriented

1 - Normal sleep

2 - Drowsy, arousable on touch or call

3 - Drowsy, arousable on painful stimulus

4 - Somnolent, difficult to arouse

Grading of Nausea:

0 - None

1 - Mild

2 - Moderate

3 - Severe

The following obstetric parameters were noted

1. Duration and frequency of uterine contractions recorded every 15 minutes.

2. Rate of cervical dilatation and progress of labour.
3. Duration of first, second and third stages of labour.
4. Mode of delivery.
5. Apgar score.

Any sign of maternal or foetal distress were taken as an indication for early termination of labour.

As the baby is born, APGAR score as noted and neonatal outcome was recorded by the paediatrician.

Statistical Tools :

The information collected regarding all the selected cases were recorded in a Master Chart. Data analysis was done with the help of computer using Epidemiological Information Package (EPI 2002).

Using this software, frequencies, percentage, mean, standard deviation, x^2 and 'p' values were calculated. A 'p' value less than 0.05 is taken to denote significant relationship.

OBSERVATION AND RESULTS

AGE DISTRIBUTION:

Primi

Analyzing the age of the parturient in the combined spinal epidural group primi group was in the range of 19 to 26 years with a mean age group of 22.58 (2.19) years. In the epidural group primi group was in the range of 18 to 26 years with a mean age group of 22.08 (2.39) years. The control group primi age was in the range of 18 yo 30 years with mean score of 23.16 (3.30) years.

Multi

In the CSEA group the multi group was in the range of 18 to 32 years with a mean age group of 25.15 (3.8) years. In the EA group multi was in the range of 20 to 31 years with a mean age group of 25.85 (2.85) years. Both the CSEA and the EA group were comparable with respect to age. In the control group multi range fell between 19 to 35 tears with an average mean of 25.72 (3.38) years. The control group was comparable to both the study groups with respect to age and the difference was statistically insignificant.

HEIGHT, WEIGHT CHARACTERISTICS:

Primi

In the CSEA group the mean height in the primi group was 152.67 (5.91) cm and the mean weight was 55.75 (10.91) kgs. In the epidural group the mean height in the primi group was 154.33 (5.42) cm and the mean weight was 56.33 (10.85) kgs. In the control group the mean height in the primi group was 151.8(6.6) cm and the mean weight was 55.52(4.37) kgs.

Multi

In the CSEA group among multi mean height and weight were 153.38 (6.09) cm and 61.69 (7.17) kgs respectively whereas in the EA group it was 154.69 (4.4) cm and 62.15 (7.85) kgs respectively and in the control group it was 153.04(4.64) cm and 54.68(6.13) kgs respectively.

Both the CSEA and EA groups were comparable with respect to height and weight. The study and control groups were comparable with respect to height and weight and the difference was statistically insignificant.

RATE OF CERVICAL DILATATION:

Primi:

The mean rate of cervical dilatation per hour in the primigravidae in CSEA group was 3.42(0.38) cm and in the EA group it was 4.22(0.52) cm. The mean rate of cervical dilatation per hour in the control group among primigravidae in was 1.63(1.04) cm.

Multi:

The mean rate of cervical dilatation per hour in the multiigravidae in CSEA group was5.97 (0.58) cm and in the EA group it was 6.03(0.62) cm. The mean rate of cervical dilatation per hour in the control group among the multi it was 2.00(1.01) cm.

The mean rate of cervical dilatation was comparable between CSEA and EA groups.

The difference in the mean rate of cervical dilatation between the control group and CSEA group was statistically significant and the difference in the mean rate of cervical dilatation between the control group and EA group was also statistically significant.

AMOUNT OF DRUGS USED:

Bupivacaine

Primi

The amount of bupivacaine (in milligrams) used in CSEA group was on an average 31.83(15.76) and in the EA group it was on an average 32.92(6.11).

Multi

The amount of bupivacaine (in milligrams) used in CSEA group on an average was 17.86(6.54) and in the EA group it was 22.5(6.85).

The difference was not significant among both primi and multi.

Fentanyl

Primi

The amount of fentanyl (in micrograms) used in CSEA group was on an average 74.3(25.25) and in the EA group it was 52.67(9.77).

Multi

The amount of fentanyl (in micrograms) used in CSEA group was on an average 50.23(8.85) and in the EA group it was 36.0(10.95).

The difference was significant among both primi and multi.

TOTAL NO OF TOP UPS GIVEN:

Primi

The average number of top ups required in primi was 2.5(1.24) in CSEA group and 2.83(0.58) in EA group.

Multi

The average number of top ups required in multi was 1.38(0.51) in CSEA group and 1.85(0.55) in EA group.

The difference was significant among both primi and multi.

ONSET OF PAIN RELIEF:

CSEA

Onset of analgesia in the CSEA group was within 1 to 2 minutes in both the primi and multi gravidae with a mean of 1.71(0.33) minutes in primi and 1.38(0.36) minutes in multi.

EA

Onset of analgesia in the EA group was within 3 to 7 minutes in both the primi and multi gravidae with a mean of 5.25(1.36) minutes in primi and 4.46(1.05) minutes in multi.

Time to get the painless uterine contraction was noted and was taken as the onset time. There was a significant difference in the onset times between the two study groups with the CSEA group having rapidity of analgesic onset as early as 1 minute post block.

QUALITY OF PAIN RELIEF:

Primi

The mean VAS score in primi of CSEA group was 1.4 (0.73) and in the EA group was 2.54(0.97).

Multi

The mean VAS score in multigravidae of CSEA group was 0.51(0.24) and in the EA group was 1.27(0.6).

On analysis of the VAS scores between the two groups there is a statistically significant difference both among primi and multi gravidae. Of greater significance is the immediate post block scores which average 0.31(0.18) in primi and 0.15(0.15) in multi of the CSEA group.

GRADING:

CSEA

Pain relief was excellent in 84%, good in 12 % and satisfactory in 4% of parturients who received CSEA.

EA

Pain relief was excellent in 52%, good in 32% and satisfactory in 16% of parturients who received EA.

BREAKTHROUGH PAIN:

Breakthrough pain occurred in 4% of parturients who received CSEA and in 16% of parturients who received EA. The difference was significant statistically ($p<0.5$).

SENSORY LEVEL:

The sensory level obtained was adequate and between T6 to T10 in both the groups.

DURATION OF LABOUR:

DURATION OF FIRST STAGE (ACTIVE PHASE) OF LABOUR:

Primi: The average duration of the first stage of labour in the primi (CSEA) group was 122.92 (45.8) minutes. The average duration of the first stage of labour in the primi (EA) group was 99.6 (15.2) minutes. The difference was statistically insignificant.

The average duration of the first stage of labour in the primi (CSEA) group was 122.92 (45.8) minutes. The average duration of the first stage of labour in the primi (Control) group was 201.47(57.78) minutes. The difference was statistically significant.

The average duration of the first stage of labour in the primi (EA) group was 99.6 (15.2) minutes. The average duration of the first stage of labour in the primi (Control) group was 201.47(57.78) minutes. The difference was statistically significant.

Multi: The average duration of the first stage of labour in the multi (CSEA) group was 70.38 (23.98) minutes. The average duration of the

first stage of labour in the multi (EA) group was 69.63 (25.84) minutes. The difference was statistically insignificant.

The average duration of the first stage of labour in the multi (CSEA) group was 70.38 (23.98) minutes. The average duration of the first stage of labour in the multi (Control) group was 145 (38.83) minutes. The difference was statistically significant.

The average duration of the first stage of labour in the multi (EA) group was 69.63 (25.84) minutes. The average duration of the first stage of labour in the multi (Control) group was 145 (38.83) minutes. The difference was statistically significant.

DURATION OF SECOND STAGE OF LABOUR:

Primi: The average duration of the second stage of labour in CSEA group was 51.5(24.97) minutes. The average duration of the second stage of labour in EA group was 46.67 (11.02) minutes. The difference was statistically insignificant.

The average duration of the second stage of labour in CSEA group was 51.5 (24.97) minutes. The average duration of the second stage of

labour in Control group was 37.85 (20.9) minutes. The difference was statistically insignificant.

The average duration of the second stage of labour in EA group was 46.67(11.02) minutes. The average duration of the second stage of labour in control group was 37.85 (20.9) minutes. The difference was statistically insignificant.

Multi

The average duration of the second stage of labour in the CSEA group was 21.46(5.29) minutes. The average duration of the second stage of labour in the EA group was 23.46(8.06) minutes. The difference was statistically insignificant.

The average duration of the second stage of labour in the CSEA group was 21.46 (5.29) minutes. The average duration of the second stage of labour in the Control group was 20.76 (12.8) minutes. The difference was statistically insignificant.

The average duration of the second stage of labour in the EA group was 23.46(8.06) minutes. The average duration of the second stage of

labour in the Control group was 20.76(12.8) minutes. The difference was statistically insignificant.

DURATION OF THIRD STAGE OF LABOUR:

The average duration of the third stage of labour was comparable among primi and multi of CSEA, EA and control groups. There was no statistically significant difference.

TOTAL DURATION OF LABOUR:

Primi : The mean total duration of labour in the CSEA group was 180.67(67.53) minutes. The mean total duration of labour in the EA group was 152.33 (26.38) minutes. The difference was statistically insignificant. The mean total duration of labour in the control group was 246.92 (24.25) minutes. The difference was statistically significant between the study and control groups.

Multi

The mean total duration of labour in the CSEA group was 96.46 (28.99) minutes. The mean total duration of labour in the EA group was 95.92 (33.32) minutes. The difference was statistically insignificant. The mean total duration of labour in the control group was 171.53(15.44)

minutes. The difference was statistically significant between the study and control group. The mean total duration of labour in the multi (EA) group was 95.92(33.32) minutes. The mean total duration of labour in the multi (Control) group was 171.53(15.44) minutes. The difference was statistically insignificant. The difference was statistically significant.

MODE OF DELIVERY:

Primi: 50% of the primi in the CSEA group had natural labour and 50% of the primi in EA group also had labour naturale. The results were comparable between the two study groups. 41.7% had instrumental delivery in CSEA group and 50% had instrumental delivery in the EA group. One primi gravida in the CSEA had caesarean delivery and none in EA group. The results were comparable and not statistically significant. 84% in the control group had labour naturale which was statistically significant when compared with those in CSEA and EA groups. Only 16.7% had instrumental delivery in the control group which again was statistically significant when compared to those in CSEA and EA groups. None had caesarean delivery in the control group which was comparable to those in the CSEA and EA groups.

Multi: 100 % of the multi in the CSEA group had natural labour and 92.3% of the multi in EA group also had labour naturale. The results were comparable between the two study groups. None had instrumental delivery in CSEA group and 7.7% had instrumental delivery in the EA group. None had caesarean delivery in either CSEA or EA group. The results were comparable and not statistically significant. 92% in the control group had labour naturale which was statistically not significant when compared with those in CSEA and EA groups. Only 8% had instrumental delivery in the control group which again was statistically not significant when compared to those in CSEA and EA groups. None had caesarean delivery in the control group which was comparable to those in the CSEA and EA groups.

INDICATIONS FOR ASSISSTED DELIVERY:

Assisted deliveries include both forceps and lower segment caesarean section deliveries. Among the primigravidae assisted delivery was required by 50% in the CSEA group and 50% in the EA group. Among the multigravidae assisted delivery was required by none in the CSEA group and by 7.7% in the EA group.

In the control group 8.3% of primigravidae required assisted delivery and 7.69% of multigravidae required assisted delivery.

APGAR SCORE:

Foetal wellbeing was assessed using the APGAR scoring done at 1 minute and 5 minutes from the time since birth. The mean APGAR in the study (CSEA, EA) and control group among both primi and multi were similar.

COMPLICATIONS:

Pruritis was the most common complication occurring during CSEA (96%) followed by sedation (84%). In the EA group 32% had pruritis and 20% had sedation. The differences were statistically significant. Nausea and vomiting occurred in 16% of CSEA group and in 12% of EA group. The difference was statistically insignificant. Shivering occurred in 24% of CSEA group, 20% of EA group and 4% of control group. The difference was statistically insignificant. Headache occurred in

8% of CSEA group and in 4% of EA group. The difference was statistically insignificant.

Backache occurred in 4% of CSEA and in 8% of control group.

Urinary retention occurred in 4% each of CSEA and EA groups.

Motor blockade occurred only in one parturient (4%) in the EA group which was of grade-1(modified bromage scale).

Hypotension occurred in 12% of CSEA and in 4% of EA group.

Incidence of respiratory depression associated with neuraxial opioids is dose dependent and typically ranges from 0.1 to 0.9% .There was no instance of respiratory depression in either of the study groups.

DISCUSSION

Pain perception by the parturient is a dynamic process that involves both the peripheral and central mechanisms and as reported on the McGill pain questionnaire, is one of the most intense pain that a woman can experience.

Regional techniques used in obstetrics provide optimal analgesia with minimal depressant effects on the mother and fetus while allowing the parturient to be awake and be able to participate in labour and delivery.

In CSEA intrathecal opioids and local anaesthetics are injected and an epidural catheter is left in place. The principle advantages of low dose CSEA in labour are speed of onset, selective neural blockade, fine tuning of block with minimal sympathetic, motor, sensory, proprioceptive block which allows walking, voiding, bearing down, flexibility – block can be easily converted to anaesthesia for operative or assisted delivery, drug dose requirement is reduced, predictable, reliable- less incidence of failures or patchy block compared to epidural alone and improved maternal satisfaction.

Bupivacaine is the most widely used long acting amide local anaesthetic drug used in obstetric analgesia. It is effective in 0.125% or greater (0.0625%) dilution when combined with opioids. It produces high quality analgesia with minimal motor block. It has low potential for cumulative toxicity and produces differential blockade.

Addition of fentanyl to bupivacaine allows the use of reduced concentrations of bupivacaine without compromising analgesia and achieves a reduction in the motor block. It is this reduction in the motor block which is a major driving force behind the use of neuraxial opioids.

All parturients in both the study groups and in the control group went in for spontaneous labour and were included in the study from the active phase of labour. Labour was augmented either with artificial rupture of membranes or oxytocin infusion as per the needs of the parturient.

AGE

Analyzing the age of the parturient both the primi and multi in the CSEA, EA and control group were comparable.

PARITY

In the multigravidae the distribution of parity was second gravidae- 10, third gravidae- 2 and fourth gravidae- 1 in both CSEA and EA groups and in the control group it was second gravidae- 9, third gravidae- 3and fourth gravidae- 1. The study and control groups were comparable.

HEIGHT AND WEIGHT DISTRIBUTION:

Both primi and multigravidae in the CSEA, EA and control group were comparable with respect to height and weight.

ANALGESIA:

CSEA: Onset of analgesia in the CSEA group was within 1 to 2 minutes in both the primi and multi gravidae with a mean of 1.71(0.33) minutes in primi and 1.38(0.36) minutes in multi.

EA: Onset of analgesia in the EA group was within 3 to 7 minutes in both the primi and multi gravidae with a mean of 5.25(1.36) minutes in primi and 4.46(1.05) minutes in multi.

VAS Score on analysis: Of the VAS scores between the two groups there is a statistically significant difference both among primi and multi

gravidae. The mean VAS score in primi of CSEA group was 1.4 (0.73) and in the EA group was 2.54(0.97). The mean VAS score in multigravidae of CSEA group was 0.51(0.24) and in the EA group was 1.27(0.6).

Of greater significance is the immediate post block scores which average 0.31(0.18) in primi and 0.15(0.15) in multi of the CSEA group. This is due to the effect of intrathecal fentanyl and it also contributes to the enhanced analgesic quality of subsequent epidural top ups due to its effects known to last for 2 to 3 hours.

Grading: Pain relief was excellent in 84%, good in 12 % and satisfactory in 4% of parturients who received CSEA, whereas pain relief was excellent in 52%, good in 32% and satisfactory in 16% of parturients who received EA.

Breakthrough pain: Occurred in 4% of parturients who received CSEA and in 16% of parturients who received EA. The difference was significant statistically ($p<0.5$).

- In a similar study conducted by A.T. Sia et al a similar observation was made with the need for supplemental analgesics being greater in

the EA group. They have stated that induction with a spinal block as in CSEA produces a faster onset and more efficacious block than EA. CSEA cold be deemed to be superior to and more uniform than EA in counteracting the increased nociception that occurs as the second stage of labour approaches, especially with respect to the contribution of the perineal afferents.

- David Hepner et al reported VAS score of < 3 within 5 minutes and the first sign of analgesia as early as 1.8(1.5) minutes, reflecting rapid onset of complete analgesia with CSEA over that of conventional epidural analgesia.
- According to Roshan Fernando in article on ambulatory epidurals he reported that the epidural technique will have a slower onset time than the CSEA but both should offer equivalent analgesia after 30 minutes.

Similar observations were made by other authors and also in our study.

AMOUNT OF BUPIVACAINE AND FENTANYL USED:

Bupivacaine

Primi and multi gravidae of CSEA and EA group were comparable and statistically insignificant.

Fentanyl

The amount of fentanyl (in micrograms) used in CSEA group among both primi and multi gravidae was significantly higher than EA group.

This is due to the initial bolus dose of 25mcg fentanyl intrathecally and initial epidural dose of 20 mcg of fentanyl remaining a constant, subsequent doses were adjusted to heart rate, blood pressure and sedation. Whereas in the EA group only the initial bolus of 20mcg of fentanyl was constant, subsequent doses being titrated according to heart rate, blood pressure and sedation.

Despite the higher dose of fentanyl used in the CSEA group no major complications to the mother or foetus occurred and had the benefit of rapid and complete analgesia leading to greater parturient satisfaction.

AT Sia et al in their study reported greater parturient satisfaction in CSEA over EA ($p < 0.026$)

MEAN RATE OF CERVICAL DILATATION:

The difference in the mean rate of cervical dilatation between the CSEA and EA groups was statistically insignificant. The difference in the

mean rate of cervical dilatation between the control group and CSEA group was statistically significant. The difference in the mean rate of cervical dilatation between the control group and the EA group was also statistically significant.

The study groups had a rapid progression of labour with good uterine contraction and cervical dilatation which is due to elimination of anxiety and pain of labour and the correction of dystocia.

DURATION OF THE FIRST STAGE OF LABOUR:

The average duration of the first stage of labour in both primi and multi in CSEA and EA group was comparable. The average duration of the first stage of labour in both primi and multi in the study groups were significantly less than the control group.

Only the active stage of labour was taken into account. Women managed actively in labour regardless of the timing of epidural placement had shorter labours than controls.(Roger R et al, 1999).

Chestnut and associates have reported that continuous infusion of 0.0625% bupivacaine with 2mcg of fentanyl given to primi did not

prolong, but tended to decrease the duration of the active phase of the first stage of labour compared to the general obstetric population.

DURATION OF SECOND STAGE OF LABOUR:

The average duration of the second stage of labour in the primi and multi gravidae in the CSEA and EA groups were marginally prolonged compared to the control group but it was not statistically significant.

DURATION OF THIRD STAGE OF LABOUR:

The average duration of the third stage of labour in the primi and multi of the CSEA, EA and control groups were comparable statistically insignificant.

TOTAL DURATION OF LABOUR:

Primi

The mean total duration of labour in the CSEA group was 180.67(67.53) minutes. The mean total duration of labour in the EA group was 152.33(26.38) minutes. The mean total duration of labour in the control group was 246.92 (24.25) minutes

Multi

The mean total duration of labour in the CSEA group was 96.46 (28.99) minutes. The mean total duration of labour in the EA group was 95.92(33.32) minutes. The mean total duration of labour in the control group was 171.53 (15.44) minutes. The total duration of labour was significantly shortened in the CSEA and EA groups among both primi and multi gravidae when compared to that of the control group.

MODE OF DELIVERY:

In the CSEA and EA groups no difference in the mode of delivery was observed in the primi and multi groups except for that the incidence of instrumental delivery was higher among the primi gravidae.

Primi: Only 12% of primi had instrumental delivery in the control group which again was statistically significant when compared to those in CSEA and EA groups. 4% had caesarean delivery in the control group which was comparable to those in the CSEA and EA groups.

MULTI: 92% in the control group had labour naturale which was statistically not significant when compared with those in CSEA and EA groups. Only 8% had instrumental delivery in the control group which again was statistically not significant when compared to those in CSEA

and EA groups. None had caesarean delivery in the control group which was comparable to those in the CSEA and EA groups.

In the study by A.T.Sia et al no difference was detected in the mode of delivery between the CSEA and EA groups.

Nageotte and colleagues in their study comparing epidural analgesia with combined spinal epidural analgesia during labour in nulliparous women found no significant difference between the two groups in terms of the rate of caesarean section or the frequency of dystocia.

INDICATION FOR ASSISTED DELIVERY:

Assisted deliveries include both forceps and lower segment caesarean section deliveries.

Primi: In the CSEA group 3 parturients underwent assisted delivery for failure of secondary forces, 1 parturient for prolonged second stage, 1 parturient for foetal distress and 1 parturient underwent caesarean section due to persistent occipito-posterior presentation. In the EA group 3 parturients underwent assisted delivery due to failure of secondary

forces and 2 parturients for foetal distress. In the control group 2 required assisted delivery for failure of secondary forces.

Multi: In the EA group one parturient required caesarean section for foetal distress and in the control group one parturient required caesarean delivery for foetal distress.

FOETAL SURVEILLANCE:

Foetal wellbeing was assessed using the APGAR scoring done at 1 minute and 5 minutes from the time since birth. The mean APGAR in the study (CSEA, EA) and control group among both primi and multi were similar.

In a study conducted by Fernando et al (1997) there was no correlation between APGAR score, umbilical blood gases or neurobehavioral scores and umbilical venous concentration of either fentanyl or bupivacaine.

SIDE EFFECTS:

Pruritis was the most common complication occurring during CSEA (96%) followed by sedation (84%). In the EA group 32% had

pruritis and 20% had sedation. The differences were statistically significant. Pruritis has an incidence of 60% with neuraxial opioid administration as compared to about 15 to 18% for epidural local anaesthetics or systemic opioids. Greater incidence of pruritis occurs during pregnancy. Mechanism of pruritis is considered to be due to central activation of the itch centre in the medulla or opioid receptors in the trigeminal nucleus or nerve roots with cephalad migration of the opioid..

Nausea and vomiting occurred in 16% of CSEA group and in 12% of EA group. The difference was statistically insignificant. Nausea and vomiting associated with neuraxial administration of single dose opioids occurs in approximately 20-50% of patients and the cumulative incidence among those receiving continuous infusions of opioids may be as high as 45% to 80%. It may be due to the cephalad migration of the opioid within the CSF to the area postrema in the medulla. Use of fentanyl in combination with local anaesthetics is associated with lower incidence of nausea and vomiting when compared with infusions using morphine.

Shivering occurred in 24% of CSEA group and in 20% of EA group. The difference was statistically insignificant.

Headache occurred in 8% of CSEA group and in 4% of EA group. The difference was statistically insignificant.

Urinary retention occurred in 4% each of CSEA and EA groups.

Motor blockade occurred only in one parturient (4%) in the EA group which was of grade-1(modified bromage scale).

Backache occurred in 4% of CSEA and in 8% of control group.

Hypotension occurred in 12% of CSEA and in 4% of EA group.

Incidence of respiratory depression associated with neuraxial opioids is dose dependent and typically ranges from 0.1 to 0.9% .There was no instance of respiratory depression in either of the study groups.

A T Sia and colleagues in their study found pruritis was more frequent in the CSEA group. Compared with EA group, the CSEA did not increase the risk of postpartum headache, backache or urinary retention. In their study EA group was associated with a higher incidence of transient neurological deficits.

SUMMARY

The study involved a total of 75 parturients, 25 in the combined spinal epidural analgesia group (CSEA), 25 in the epidural analgesia group (EA) and 25 in the control group. There were 12 primi and 13 multigravidae in each group.

Labour analgesia using above techniques was provided once the parturient entered the active phase of labour.

CSEA group received an initial intrathecal fentanyl 25 mcg with 0.5ml of preservative free bupivacaine 0.25%. It was followed by maintenance with intermittent boluses of 10ml of 0.125% bupivacaine with 2mcg/ml of fentanyl hourly starting from 45 minutes after the intrathecal dose.

EA group received 10ml of 0.125%bupivacaine with 2mcg/ml of fentanyl hourly from the time of initiation.

Onset of analgesia CSEA group was a mean of 1.71 (0.33) minutes in primi and 1.38 (0.36) minutes in multi as against a mean of 5.25 (1.36) minutes in primi and 4.46 (1.05) minutes in multi in EA group. There was

a significant difference in the onset times with the CSEA group having rapidity of analgesic onset as early as 1 minute post block.

Labour analgesia was excellent in 84% of parturients, good in 12% and satisfactory in 4% in CSEA group as opposed to 52% excellent, 32% good and 16% satisfactory response in EA Group.

The mean rate of cervical dilatation was comparable in both the groups. The mean duration of first, second and third stages of labour among primi and multi in CSEA and EA group were comparable and not statistically significant. When compared to the control group there was significantly greater rate of cervical dilatation leading to rapid progression of first stage of labour in the study group. The average duration of second stage of labour was marginally prolonged in the study groups when compared to the control group but were statistically insignificant. The average duration of the third stage of labour was comparable between the study and control groups. There was a significant reduction in the total duration of labour in the CSEA & EA groups when compared to the study group.

The mean amount of bupivacaine used in primi and multigravidae in CSEA and EA group were similar and not statistically significant. The mean amount of fentanyl used in primi and multigravidae in CSEA group was higher when compared to the amount used in EA group in both primi and multigravidae but with no major side effects to the mother or foetus.

CSEA was associated with greater parturient satisfaction.

The mode of delivery was comparable between CSEA and EA among both primi and multigravidae. The difference in the mode of delivery was statistically insignificant between the two groups.

The incidence of instrumental delivery was higher in primipara of both CSEA and EA groups when compared to control.

First minute Apgar scores in the neonate was 6.8(0.7) and 6.56(0.65) in the CSEA and EA groups respectively. 5^{th} minute Apgar score in the neonate was 8.56(0.58) and 8.36(0.57) in the CSEA and EA groups respectively. The results were not statistically significant.

Pruritis was the most frequently reported side effect with CSEA followed by nausea, vomiting and sedation. These were statistically

higher than those observed in EA group. Pruritis was mild and short lived requiring no intervention. Other side effects like headache, shivering, hypotension were observed to a lesser and comparable extent among both CSEA and EA groups. There were no major maternal or foetal complications with either CSEA or EA techniques.

CONCLUSION

Combined spinal epidural analgesia with fentanyl – bupivacaine combination is associated with greater parturient satisfaction due to its rapidity of onset providing complete pain relief in 1.54minutes on an average. The quality of pain relief was excellent in 84% of parturients with very less requirement for supplemental analgesics. In the above respect CSEA was far superior compared to EA.

CSEA has a favourable outcome on the progress of labour. It augments cervical dilatation and shortens the first stage of labour by producing good co-ordinated uterine contractions at regular intervals. The duration of the second stage of labour was prolonged without any maternal or foetal complications. Neonatal outcome was favourable as evidenced by the 1minute and 5 minute APGAR scores. The above effects were comparable to conventional group.

Though the incidence of pruritis, sedation, nausea and vomiting were higher they were either transient or mild requiring no intervention. No major maternal or foetal complications occurred reflecting the safety profile of a properly conducted CSEA.

Combined spinal epidural analgesia with fentanyl – bupivacaine combination is thus a safe and better alternative to EA as a technique of neuraxial block for effective labour analgesia.

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PROFORMA

COMPARISON OF COMBINED SPINAL EPIDURAL ANALGESIA WITH EPIDURAL ANALGESIA USING FENTANYL- BUPIVACAINE COMBINATION FOR EFFECTIVE LABOUR ANALGESIA

Date

S.No
CSEA/ EA/Control No.
IP.No
Unit
Obstetric Assistant

Name

Age

Height

Anesthesiology Asst

Weight

Parity

History

Basic Investigations

O/E	Maternal	Fetal
	General condition	Heart rate
	CVS	
	RS	
	CNS	
	P/A	
	P/V	

Pre Block Maternal Fetal

Pulse Rate Heart Rate

Blood Pressure

SpO2

Respiratory Rate

Cervical Dilatation

Pain Score

Oxytocin Use

Block

Technique

Start Time

Problems

First Dose

Time PR BP SpO2 RR FHR

Uterine Activity

Pain relief – Score

Motor Block

Sedation Score

Other adverse reactions (Time and Intervention)

Labour Progress

Obstetric intervention

Top Up 1

Time PR BP SpO2 RR FHR

Uterine Activity

Pain relief – Score

Motor Block

Sedation Score

Other adverse reactions (Time and Intervention)

Labour Progress

Obstetric intervention

Top up II

Time PR BP SpO2 RR FHR

Uterine Activity

Pain relief – Score

Motor Block

Sedation Score

Other adverse reactions (Time and Intervention)

Labour Progress

Obstetric intervention

Further Top ups were recorded in a similar manner as above.

Delivery

Time

Mode

Episiotomy

Monitoring

Duration

I stage

II stage

Follow up	Maternal	Fetal
	Headache	Birth Weight
	Transient Neurological deficit	APGAR – 1 minute
		5 minute
	Urinary retention	
	Overall parturient satisfaction	

Queen Victoria

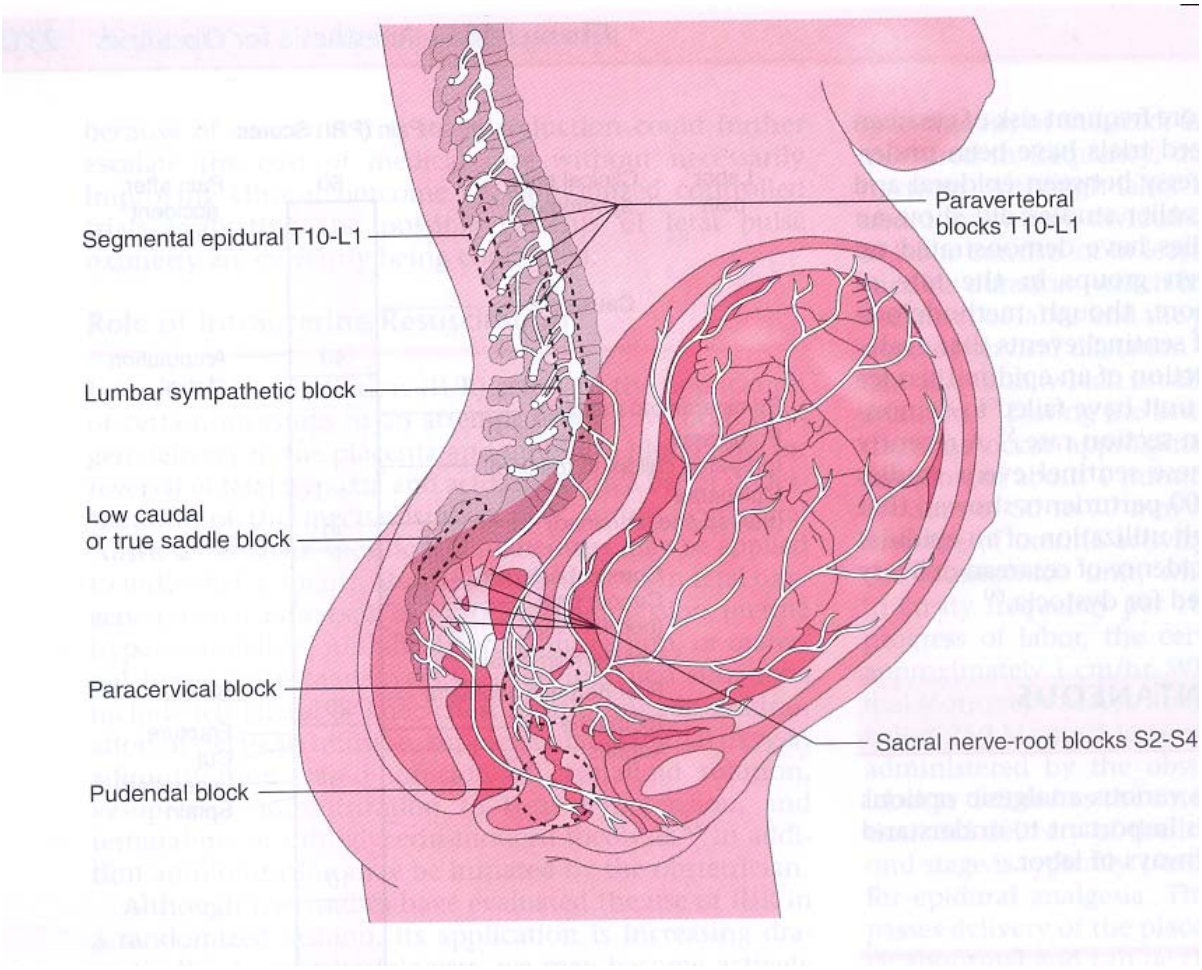
(born 1819, reigned 1839 - 1901)

"Doctor Snow gave that blessed chloroform and the effect was soothing, quieting, and delightful beyond measure."

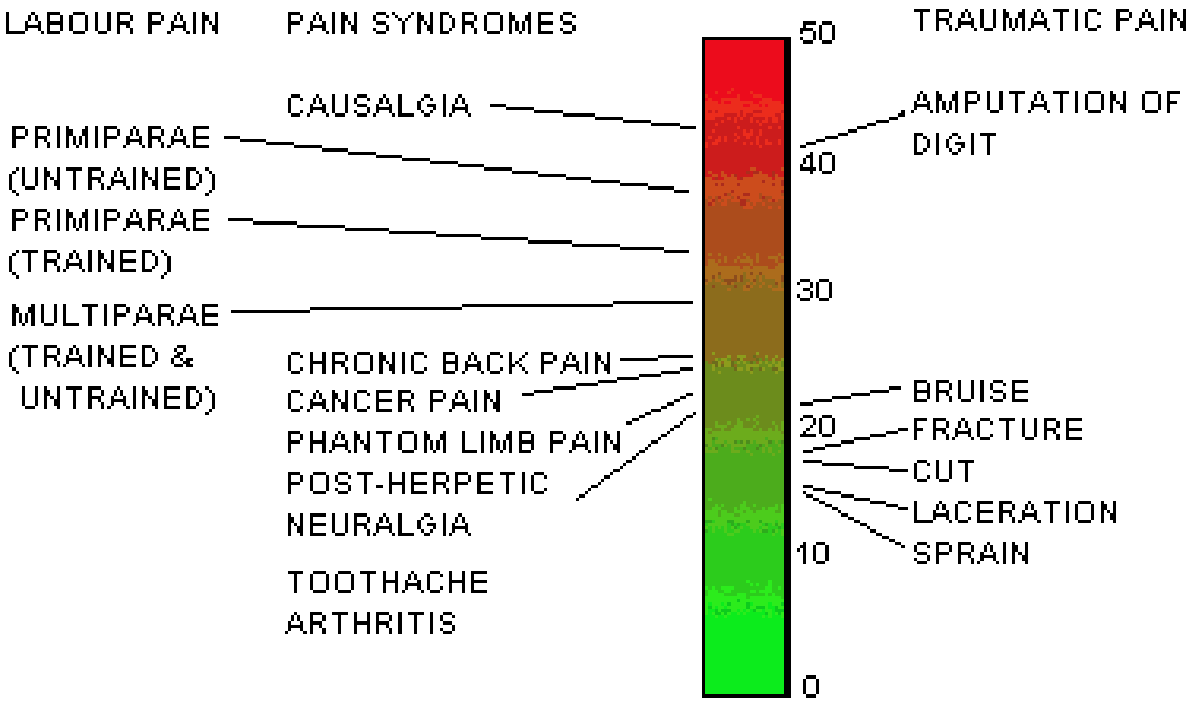
Professor James Young Simpson
(1811 – 1870)

"All pain is* per se *and especially in excess, destructive and ultimately fatal in its nature and effects."

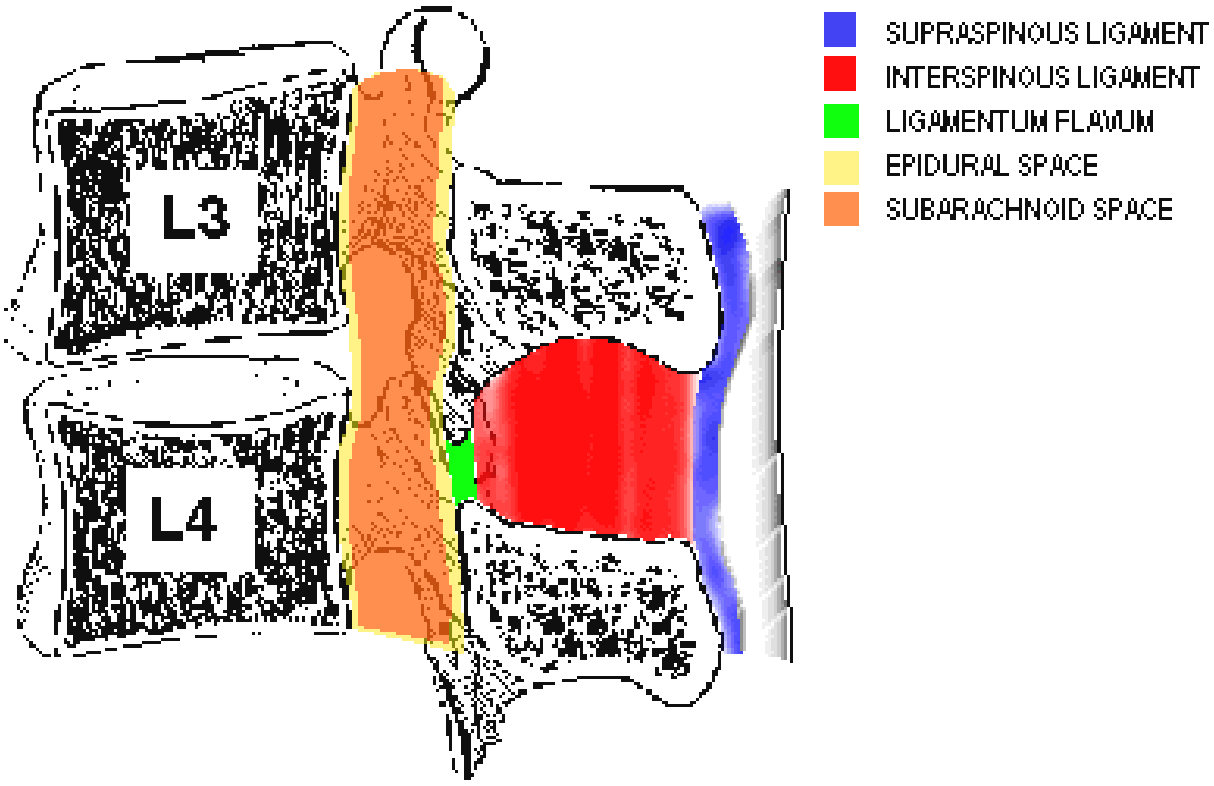
PATHWAYS OF LABOUR PAIN AND TYPES OF BLOCKS FOR PAIN RELIEF



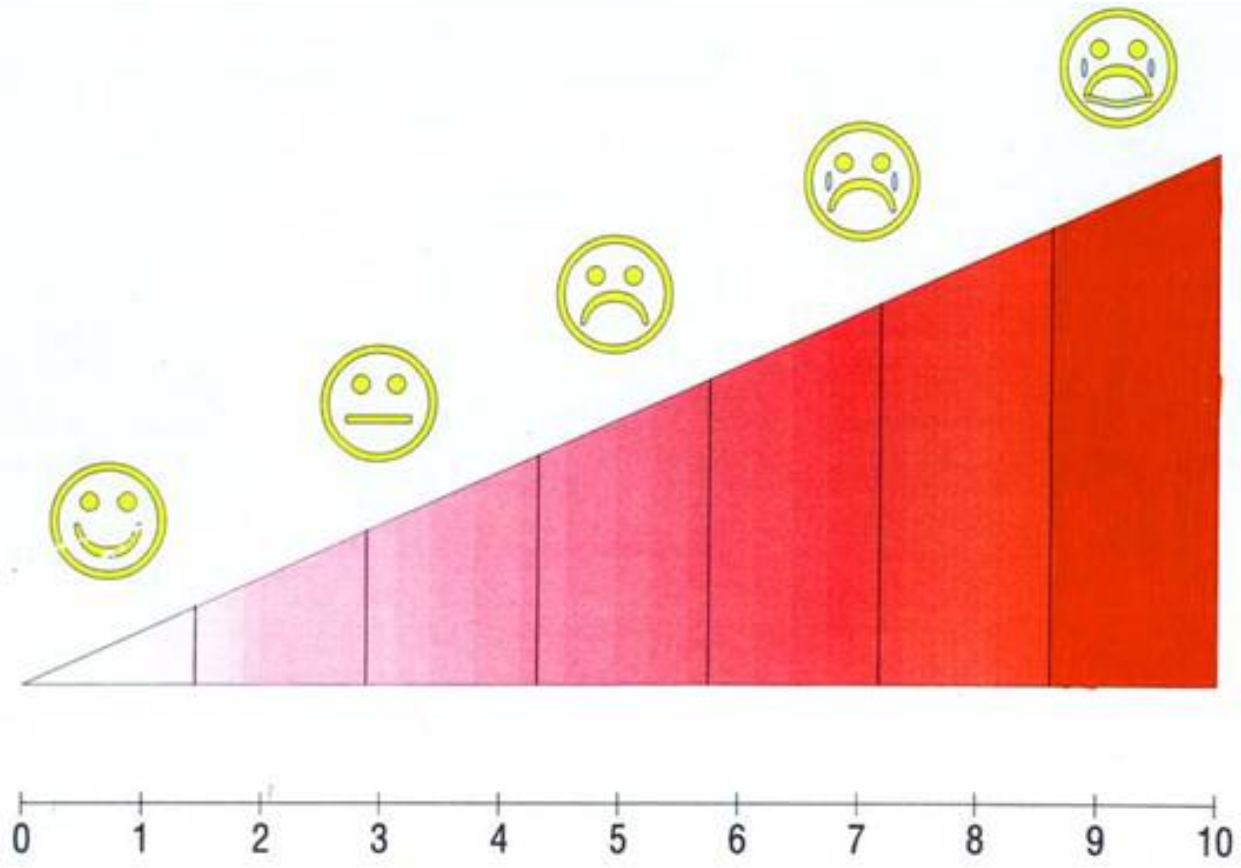
Mc Gills Pain Rating Index - Scores



ANATOMY OF SPINAL – EPIDURAL SPACE

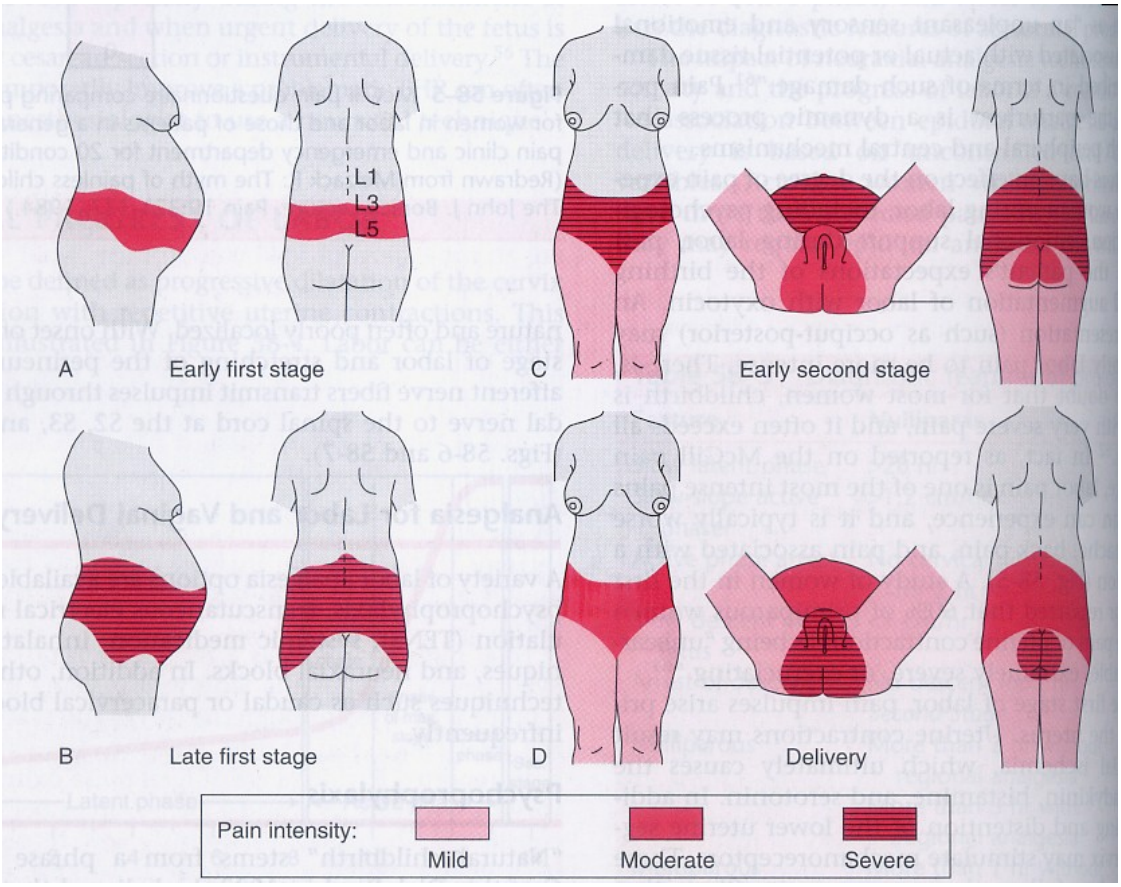


VISUAL ANALOGUE SCALE
Pain Score

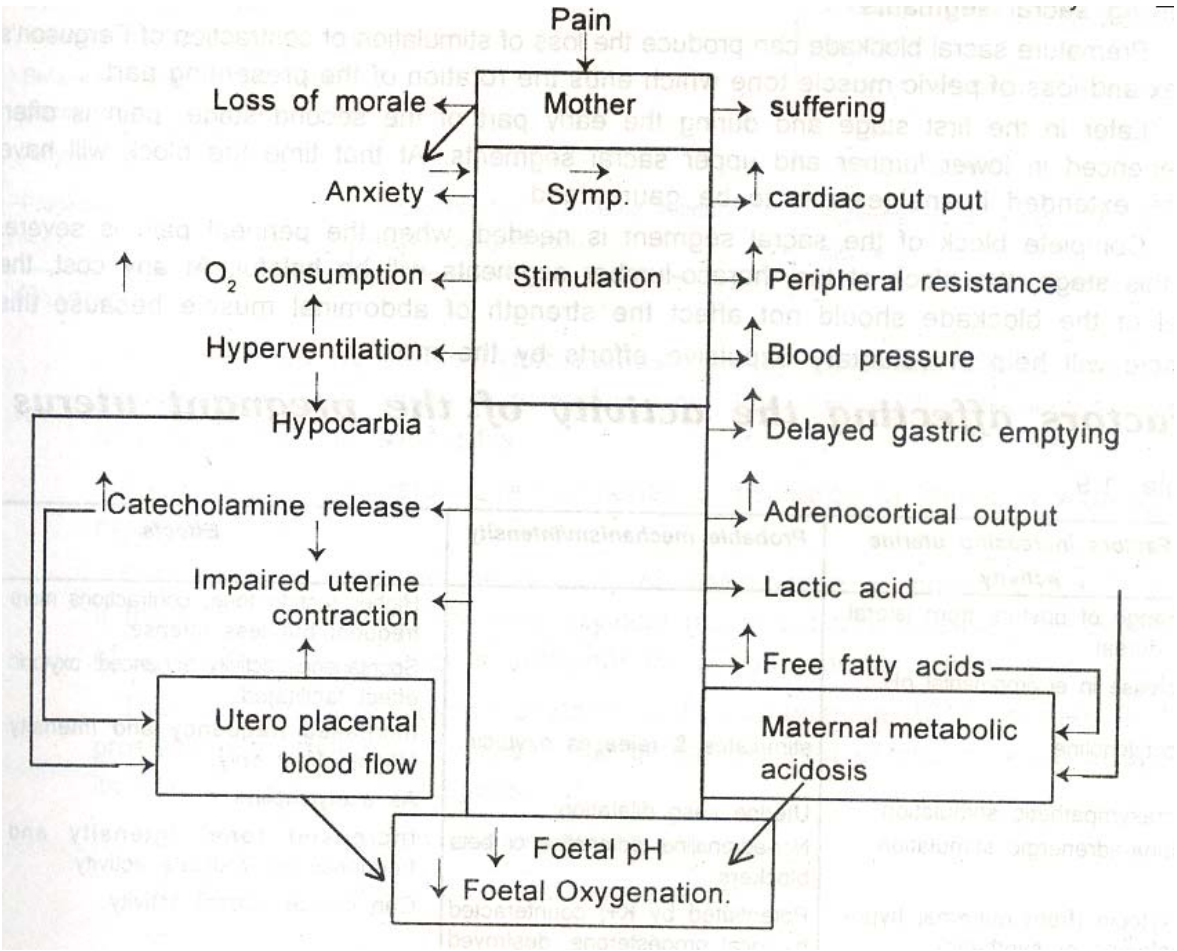


VAS	QUALITY OF ANALGESIA
0-2	Excellent
3-4	Good
4-6	Satisfactory
6-8	Slight
8-10	No relief

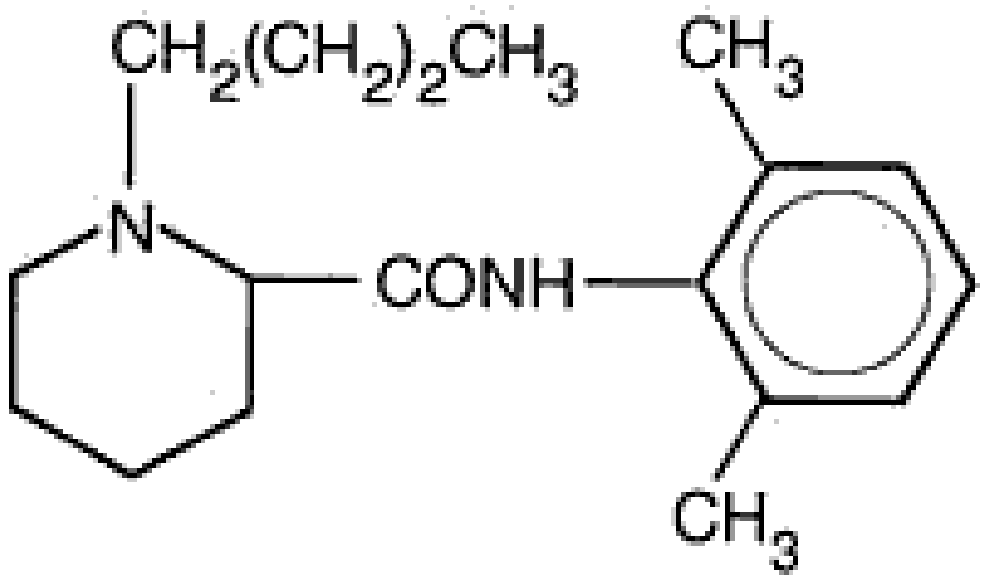
DISTRIBUTION AND INTENSITY OF LABOUR PAIN DURING EACH STAGE OF LABOUR AND DELIVERY



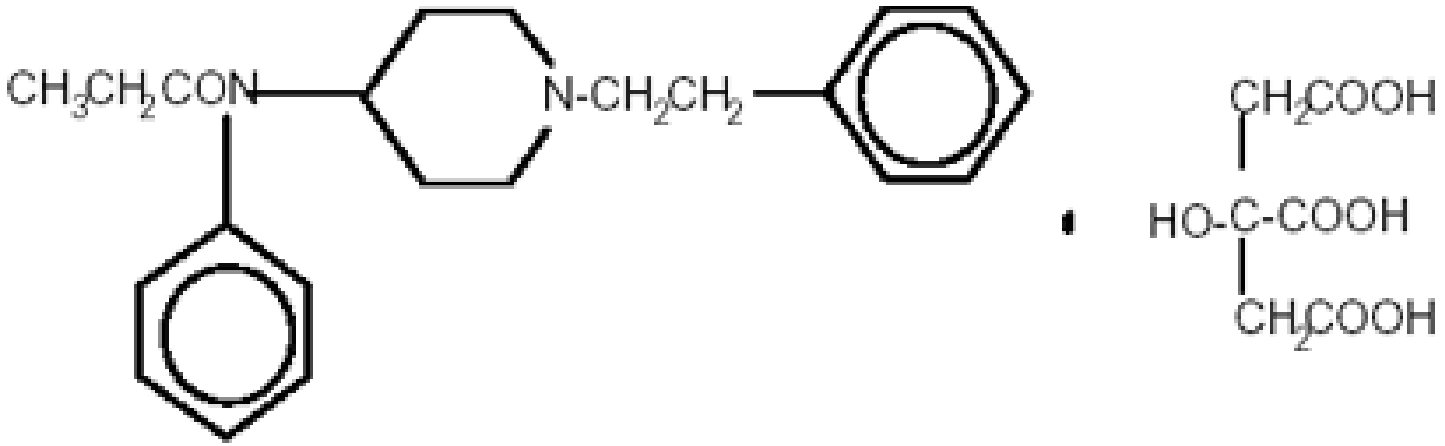
CONSEQUENCES OF UNRELIEVED PAIN IN LABOUR



BUPIVACAINE STRUCTURAL FORMULA



FENTANYL STRUCTURAL FORMULA



AGE DISTRIBUTION:

Category	Age in years				
	CSEA		EA		'p'
	Mean	S.D.	Mean	S.D.	
Primi	22.58	2.19	22.08	2.39	0.5799 Not significant
Multi	25.15	3.8	25.85	2.85	0.518 Not significant

Category	Age in years				
	CSEA		CONTROL		'p'
	Mean	S.D.	Mean	S.D.	
Primi	22.58	2.19	23.16	3.30	0.5801 Not significant
Multi	25.15	3.8	25.72	3.38	0.522 Not significant

Category	Age in years				
	EA		CONTROL		'p'
	Mean	S.D.	Mean	S.D.	
Primi	22.08	2.39	23.16	3.30	0.6123 Not significant
Multi	25.85	2.85	25.72	3.38	0.5231 Not significant

HEIGHT, WEIGHT CHARACTERISTICS:

Parameter	CSEA		EA		'p'
	Mean	S.D.	Mean	S.D.	
Height (in cms)					
Primi	152.67	5.91	154.33	5.42	0.2123 (Not significant)
Multi	153.38	6.09	154.69	4.4	0.4241(Not significant)
Weight (in kgs)					
Primi	55.75	10.91	56.33	10.85	0.8848 (Not significant)
Multi	61.69	7.17	62.15	7.85	0.8357(Not significant)

Parameter	CSEA		CONTROL		'p'
	Mean	S.D.	Mean	S.D.	
Height (in cms)					
Primi	152.67	5.91	151.80	6.6	0.4217(Not significant)
Multi	153.38	6.09	153.04	4.64	0.6721(Not significant)
Weight (in kgs)					
Primi	55.75	10.91	55.52	4.37	0.8912 (Not significant)
Multi	61.69	7.17	54.68	6.13	0.2017(Not significant)

Parameter	EA		CONTROL		'p'
	Mean	S.D.	Mean	S.D.	
Height (in cms)					
Primi	154.33	5.42	151.80	6.6	0.1821(Not significant)
Multi	154.69	4.40	153.04	4.64	0.4210(Not significant)
Weight (in kgs)					
Primi	56.33	10.85	55.52	4.37	0.7612(Not significant)
Multi	62.15	7.85	54.68	6.13	0.0714(Not significant)

RATE OF CERVICAL DILATATION:

Category	Rate of Cervical Dilatation (in cms)				
	CSEA		EA		'p'
	Mean	S.D.	Mean	S.D.	
Primi	3.42	0.38	4.22	0.52	0.2248 Not significant
Multi	5.97	0.58	6.03	0.62	0.8776 Not significant

Category	Rate of Cervical Dilatation (in cms)				
	CSEA		CONTROL		'p'
	Mean	S.D.	Mean	S.D.	
Primi	3.42	0.38	1.63	1.04	0.021 Significant
Multi	5.97	0.58	2.00	1.01	0.014 Significant

Category	Rate of Cervical Dilatation (in cms)				
	EA		CONTROL		'p'
	Mean	S.D.	Mean	S.D.	
Primi	4.22	0.52	1.63	1.04	0.0061 Significant
Multi	6.03	0.62	2.00	1.01	0.0093 Significant

AMOUNT OF DRUGS USED:

Drug	CSEA		EA		'p'
	Mean	**S.D.**	**Mean**	**S.D.**	
Bupivacaine (mg)					
Primi	31.83	15.76	32.92	6.11	0.3845(Not significant)
Multi	17.86	6.54	22.5	6.85	0.2636(Not significant)
Fentanyl (μcg)					
Primi	74.3	25.25	52.67	9.77	**0.0017 (Significant)**
Multi	50.23	8.85	36.00	10.95	**0.0001(Significant)**

TOTAL NO OF TOP UPS GIVEN:

Category	Number of top ups				
	CSEA		EA		
	Mean	S.D.	Mean	S.D.	'p'
Primi	2.5	1.24	2.83	0.58	0.0413**(Significant)**
Multi	1.38	0.51	1.85	0.55	**0.0407 (Significant)**

ONSET OF PAIN RELIEF:

Category	Onset of pain relief (in minutes)				
	CSEA		EA		'p'
	Mean	S.D.	Mean	S.D.	
Primi	1.71	0.33	5.25	1.36	**0.0001(Significant)**
Multi	1.38	0.36	4.46	1.05	**0.0001(Significant)**
Total	1.54	0.38	4.84	1.25	**0.0001(Significant)**

QUALITY OF PAIN RELIEF:

Visual Analogue Scale	CSEA		EA		'p'
	Mean	S.D.	Mean	S.D.	
Initial 45 minutes					
Primi	0.31	0.18	-	-	-
Multi	0.15	0.15	-	-	-
Total	0.23	0.18	-	-	-
After first 45 minutes					
Primi	2.47	1.4	-	-	-
Multi	0.83	0.32	-	-	-
Total	1.61	1.28	-	-	-
Total average					
Primi	1.4	0.73	2.54	0.97	**0.0022 Significant**
Multi	0.51	0.24	1.27	0.6	**0.0005 Significant**
Total	0.94	0.69	1.88	1.01	**0.0003 Significant**

BREAKTHROUGH PAIN:

Break through pain	CSEA		EA	
	No.	%	No.	%
Present	1	4	4	16
Absent	24	96	21	84
Total	25	100	25	100

p = 0.032, significant

SENSORY LEVEL:

Sensory Level	CSEA		EA	
	No.	%	No.	%
T6	5	20	3	12
T7	-	-	-	-
T8	15	60	18	72
T9	-	-	-	-
T10	5	20	4	16
Total	25	100	25	100

DURATION OF LABOUR:

Stage	Duration of labour (in minutes)				
	CSEA		EA		
	Mean	S.D.	Mean	S.D.	'p'
Stage I					
Primi	122.92	45.8	99.6	15.20	0.1482 (Not significant)
Multi	70.38	23.98	69.63	25.84	0.7973(Not significant)
Stage II					
Primi	51.5	24.97	46.67	11.02	0.8618 (Not significant)
Multi	21.46	5.29	23.46	8.06	0.7799(Not significant)
Stage III					
Primi	6.82	1.66	6.7	1.4	0.361(Not significant)
Multi	4.62	0.96	3.85	1.28	0.0503(Not Significant)
Total duration					
Primi	180.67	67.53	152.33	26.38	0.3122(Not significant)
Multi	96.46	28.99	95.92	33.32	0.9653(Not significant)

DURATION OF LABOUR:

Stage	Duration of labour (in minutes)				
	CSEA		CONTROL		
	Mean	S.D.	Mean	S.D.	'p'
Stage I					
Primi	122.92	45.8	201.47	57.78	0.0011 (Significant)
Multi	70.38	23.98	145	38.83	0.0023 (Significant)
Stage II					
Primi	51.5	24.97	37.85	20.9	0.3170 (Not significant)
Multi	21.46	5.29	20.76	12.8	0.5374 (Not significant)
Stage III					
Primi	6.82	1.66	7.6	3.3	0.7832 (Not significant)
Multi	4.62	0.96	5.76	2.4	0.6914 (Not Significant)
Total duration					
Primi	180.67	67.53	246.92	24.25	0.0097 (Significant)
Multi	96.46	28.99	171.53	15.44	0.0063 (Significant)

DURATION OF LABOUR:

Stage	Duration of labour (in minutes)				
	EA		CONTROL		
	Mean	S.D.	Mean	S.D.	'p'
Stage I					
Primi	99.6	15.20	201.47	57.78	0.0027 (Significant)
Multi	69.63	25.84	145	38.83	0.0013 (Significant)
Stage II					
Primi	46.67	11.02	37.85	20.9	0.0793 (Not significant)
Multi	23.46	8.06	20.76	12.8	0.1021 (Not significant)
Stage III					
Primi	6.7	1.4	7.6	3.3	0.0925 (Not significant)
Multi	3.85	1.28	5.76	2.4	0.0839 (Not Significant)
Total duration					
Primi	152.3	26.38	246.92	24.25	0.0031 (Significant)
Multi	95.92	33.32	171.53	15.44	0.0019 (Significant)

MODE OF DELIVERY:

Mode of delivery	CSEA		EA		CONTROL	
	No.	%	No.	%	No.	%
Primi						
Labour Natural	6	50.0	6	50.0	10	83.3
LMC	2	16.7	2	16.7	-	-
Outlet	3	25.0	4	33.3	1	8.3
Instrumental Total	5	41.7	6	50.0	1	8.3
Caesarean	1	8.3	-	-	-	-
Total	12	100	12	100	12	100
Multi						
Labour Natural	13	100	12	92.3	12	92.3
LMC	-	-	-	-	-	-
Outlet	-	-	1	7.7	1	7.69
Instrumental Total	-	-	1	7.7	1	7.69
Caesarean	-	-	-	-	-	-
Total	13	100	13	100	13	100

INDICATIONS FOR ASSISSTED DELIVERY:

Indication	**CSEA**	**EA**	**CONTROL**
	No.	**No.**	**No.**
Failure of secondary forces	3	5	1
Fetal distress	1	2	1
Prolongation of II Stage	1	-	-
ROP – Non progression and fetal distress	1	-	-
Total no requiring assistance	6	7	2
Nil assistance required	19	18	23

APGAR SCORE:

Apgar Score	CSEA		EA	
	No.	**%**	**No.**	**%**
1 minute Mean S.D.	 6.8 0.7		 6.56 0.65	
'p'	0.0888 (Not significant)			
5th minute Mean S.D.	 8.56 0.58		 8.36 0.57	
'p'	0.1869 (Not significant)			

Apgar Score	CSEA		CONTROL	
	No.	**%**	**No.**	**%**
1 minute Mean S.D.	 6.8 0.7		 6.75 0.6	
'p'	(Not significant)			
5th minute Mean S.D.	 8.56 0.58		 8.4 0.61	
'p'	(Not significant)			

Apgar Score	EA		CONTROL	
	No.	**%**	**No.**	**%**
1 minute Mean S.D.	 6.56 0.65		 6.75 0.6	
'p'	(Not significant)			
5th minute Mean S.D.	 8.36 0.57		 8.4 0.61	
'p'	(Not significant)			

COMPLICATIONS:

Complications	**CSEA**		**EA**		**CONTROL**	
	No.	**%**	**No.**	**%**	**No.**	**%**
Pruritis						
Present	24	96	8	32		
Absent	1	4	17	68		
'p'	**0.0001 (Significant)**					
Shivering						
Present	6	24	5	20	1	4
Absent	19	76	20	80	24	96
'p'	0.2087 (Not significant)					
Sedation						
Present (25- Score 2 1 - score 1)	21	84	5	20		
Absent	4	16	20	80		
'p'	**0.0001 (significant)**					
Nausea						
Present	4	16	3	12		
Absent	21	84	22	88		
'p'	0.1173 (Not significant)					
Vomiting						
Present	3	12	3	12		
Absent	22	88	22	88		
'p'	0.0063 (Significant)					

Headache Present Absent	 2 23	 8 92	 1 24	 4 96		
‘p’						
Backache Present Absent	 1 24	 4 96	 2 23	 8 92	 2 23	 8 92
‘p’						
Urinary retention Present Absent	 1 24	 4 96	 1 24	 4 96	 2 23	 8 92
‘p’						
Hypotension Present Absent	 3 22	 12 88	 4 21	 16 84	 2 23	 8 92
‘p’						
Motor blockade Present (Modf.bromage I) Absent	 - -	 - -	 1 24	 4 96	 - -	 - -
‘p’						
Respiratory depression Present Absent	 - -	 - -	 - -	 - -	 - -	 - -
‘p’						

PAIN IN LABOUR : PATHWAYS & MECHANISMS

Site of origin	Characteristic Stimulus	Neural involvement	Localization
Uterus	Contraction -? Ischemic? Plus acute stretch	Sympathetic out flow, root values T11/T12 spreading to T10 & L1	Referred to anterior rami of somatic roots; upper abdominal wall anteriorly down to groin; inner aspects upper thighs.
Peri-uterine tissues mainly posterior	Pressure-either with contraction or persistent. Usually associated with foetal malposition or unusual conformation of sacrum	Somatic roots of lumbo – sacral plexus	Distribution of posterior low and mid back; also back of thighs
Lower birth canal	Distention of vagina and perineum in second stage	Somatic roots S2/3/4	Accurate to site of stimulus- not referred
Bladder	Over- distension; can be persistent or felt during contraction	Sympathetic T11-? L2 via hypogastric plexus, parasympathetic	Usually supra pubic only; rarely referred to distribution of somatic sacral roots.
Myometrium and uterine visceral peritoneum	Abruption; scar dehiscence	T10 – L1	Accurate to surface marking of site of pathology.